The Journal of Pediatrics

VOL. 7 NOVEMBER, 1935 No. 5

Original Communications

SPLENOMEGALY IN CHILDREN WITH EARLY HEMATEMESIS

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IN 1927 one of us (R. M. S.) with Howard[1] reported five children with splenomegaly in whom the first symptom of disease was severe gastric hemorrhage. We called attention to the clear-cut and characteristic clinical picture presented by this group and indicated our belief as to the probable underlying pathologic lesion. In this communication we are presenting the results of further study of these patients and observations on ten other children with the same condition seen since the time of the first report.

A survey of the literature under the titles of "Splenic Anemia," "Banti's Disease," "Splenomegaly," and "Thrombophlebitis of the Veins of the Portal System," discloses many cases similar to those which we are reporting. They are not, however, differentiated as belonging to a distinct group with special distinguishing features. The children whom we are discussing present a well-defined clinical entity characterized by splenomegaly, early hematemesis accompanied by diminution in the size of the spleen, increase in the size of the spleen with the restoration of blood loss, normal blood except immediately after hemorrhage, and a nonprogression of the disease to cirrhosis of the liver and ascites.

Hematemesis.—The association of hematemesis with splenomegaly has been recognized for many years. The first reported case is by Morgagni,[2] and his patient was much like those in our group. Banti[3] in 1894 described a triad of physical signs which has since borne his

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Read at the Meeting of the American Pediatric Society held at Cleveland, Ohio, May 2, 3, and 4, 1935.

name—splenomegaly, liver cirrhosis, and thrombophlebitis of the portal vein—and in these patients also hemorrhage occurred but late in the course of the disease. Osler[4] in 1900 and 1902, under the title of "Splenic Anemia," stimulated interest in this condition and particularly emphasized the importance of recurring hemorrhages. A voluminous literature has accumulated.[5] The feature to which we wish to call attention in our group is that without a history of recent ill health, severe gastric hemorrhage occurs as the first warning of disease. Physical examination made immediately following the hemorrhage may disclose no enlargement of the spleen. It is only after the bleeding has stopped or after transfusion that the spleen becomes palpable. In instances in which the spleen is palpable on the initial examination, the size subsequently is markedly increased. Repeated hemorrhages are common and with each recurrence of severe or continued bleeding the spleen diminishes in size and often cannot be felt but returns to its former or even to a greater size with recovery from the blood loss. Unless one is familiar with the importance of this diminution in the size of the spleen following hematemesis an explanation for the bleeding may be attributed to some other cause and the correct diagnosis missed. This was true in some of the admissions in our early cases. Opitz[6] called attention to this phenomenon in 1924, but its significance has not been appreciated.

Blood.—The blood picture in this group of children is normal except after hemorrhage. At this time it presents the findings of an anemia secondary to blood loss. There is no persisting anemia although parents often complain that the children are pale; there is no leucopenia, and the percental distribution of the white blood cells is normal. The platelet count is not elevated. A single examination of the blood made soon after a hemorrhage may be misleading, but repeated blood studies when the children are in good health will show that the blood is normal in every respect. Blackfan, Diamond, and Baty[7] call attention to this in their article in the Oxford Monographs, and further detailed study of the blood in our cases by Diamond[8] confirms the earlier statement (see Table I).

Course.—We have followed some of our cases for eight and ten years. The oldest patient is now eighteen years of age. Although none of them have reached adult life, so far as information is available from our own cases and from a study of the literature, children with splenomegaly who have early hematemesis do not develop cirrhosis of the liver and ascites which have been described as terminal features of Banti's Disease.

TABLE I

BLOOD EXAMINATIONS

PATIENT	TIME	R.B.C.	HGB %	W.B.C.	DIFFERENTIAL		
					POLY-MORPHS	LYMPHO-CYTES	MONO-CYTES
(1) E. C.	During attack	2,700,000	54	7,400			
	Between attacks	4,600,000	83	5,000	normal	normal	normal
(2) J. D.	During attack	1,850,000	30	9,600	72	20	8
	After splenectomy, in good health	4,300,000	72	8,700	normal	normal	normal
	During attack	1,200,000	18	31,000	88	10	2
(3) H. R.	During attack	1,700,000	30	6,100	61	30	9
	After splenectomy, in good health	4,600,000	85	10,200	49	47	4
(4) G. S.	During attack	1,600,000	25	5,600	49	46	5
	Between attacks, after splenectomy	4,200,000	69	9,000	54	40	6
(6) L. M.	During attack	1,200,000	15	9,700	79	18	2
(7) D. L.	During attack	1,800,000	36	7,200	63	32	3
	After splenectomy, in good health	5,200,000	71	10,800	63	35	2
(8) L. McD.	During attack	2,600,000	42	21,000	88	11	1
(9) L. C.	During attack	1,700,000	24	10,800	86	12	2
(10) M. L.	Between attacks	4,400,000	64	7,200	68	24	8
	During attack	2,200,000	30	11,500	71	22	7
(12) S. D.	During attack	2,200,000	24	7,700	69	26	5
	After splenectomy, in good health	5,000,000	66	11,800	75	18	7
(14) E. W.	During attack	2,100,000	20	8,500	54	40	6
	After splenectomy, in good health	4,600,000	60	12,800	62	29	9
(15) M. B.	During attack	3,100,000	40	2,100	90	8	2
	After splenectomy, in good health	4,800,000	73	7,800	63	17	20
	During attack	3,100,000	40	17,100	82	15	3

CASE HISTORIES

CASE 1.—Normal infancy, tonsillitis, five months later hematemesis, spleen not felt, recovery, spleen palpable, recurrences of hemorrhage, low blood platelets, death from hemorrhage.

E. C. (C. H. No. 63429, case previously reported), female, born Feb. 26, 1918, was first admitted to the hospital on Sept. 20, 1923. Her infancy was normal. She had no illness until five months before entering the hospital when she had tonsillitis. The day before admission, at five and one-half years of age, she suddenly complained of abdominal pain and vomited a large amount of clotted blood, estimated at one pint. The next day she vomited a "cupful" of dark, clotted blood. The initial physical examination revealed nothing remarkable except pallor. The spleen was not palpable. The blood showed a secondary anemia but was otherwise normal. She was transfused and had an uneventful convalescence. Two weeks later the spleen was found to be enlarged and two months later was palpable 2 cm. below the costal margin and remained at this size. She was well except for occasional pain in the abdomen until five years after the first hematemesis when she had an attack of abdominal pain and vomited a large amount of bright and clotted blood. On admission to the hospital the spleen could not be felt, but two days later it was palpable 2 cm. below the costal margin. The blood platelet count was low. She recovered quickly from this hemorrhage and remained well for two months when

she had another hemorrhage and the spleen was reduced in size to 1 cm. below the costal margin. Six months later, even though she had had no further vomiting of blood, the spleen could not be felt. On Aug. 26, 1929, one year after the hemorrhage, she had another attack of vomiting, and three weeks later the spleen was palpable three fingerbreadths below the costal margin. On Dec. 18, 1930, during a severe hematemesis, she died on the way to the hospital. No autopsy was performed.

CASE 2.—Normal infancy, scarlet fever, palpable spleen, at three years, hematemesis, spleen not felt, transfusion, spleen felt, recurrent hemorrhage, splenectomy, recurrent hemorrhage, death from hemorrhage, necropsy.

J. D. (C. H. No. 101448, case previously reported), female, was born March, 1924, and was first admitted to the hospital on Jan. 19, 1927. She was well as an infant. She had scarlet fever at one year of age, and soon after that her family physician found that she was pale and had an enlarged spleen. A provisional diagnosis of malaria was made, and intermittently for three years she received iron and quinine. Two weeks before admission to the hospital, at three years of age, she became restless and vomited "half a cupful" of dark, clotted blood. She had a second hemorrhage of about the same amount of blood just before admission to the hospital. At that time she was pale and prostrated. The spleen was not palpable. The platelet count was reduced. Two days after the hemorrhage, following transfusion, the spleen was palpable 4 cm. and two months later 5 cm. below the costal margin. She was readmitted to the hospital ten months later. One week previously she became weak and drowsy and passed tarry stools. On one occasion she vomited a small amount of bright blood. Examination at that time showed the spleen much smaller than at the time of discharge after the first entry. She improved rapidly, and at the end of two weeks splenectomy was done by Dr. W. E. Ladd. The spleen showed splenomegaly and fibrosis. She had an uneventful convalescence. She was admitted to the hospital for the third time four months later with the history that two months before she had tarry stools and one week before admission had vomited a large amount of blood. Vomiting continued while she was in the hospital and could not be controlled despite transfusions and other treatment. She died on the third day. A necropsy was obtained.

The portal vein was definitely narrowed. No varices were found in the esophagus. A number of hemorrhagic areas and several dilated veins were found beneath the mucosa near the cardiac end of the stomach. Microscopic examination of the liver showed no periportal fibrosis. In the microscopic examination of the spleen, removed four and one-half months before death, representative sections were taken from various parts of the organ, but the region of the pedicle was not sectioned. The small branches of the splenic vein were, therefore, not studied. Conclusive evidence of splenic vein obstruction was not obtained in this case, but obstruction cannot be ruled out because of incomplete investigation of all parts of the splenic vein.

CASE 3.—Omphalitis, and sepsis, digestive disturbances, palpable spleen at two years and nine months of age, hematemesis, spleen not felt, platelets low, transfusion, spleen felt, splenectomy, well for eight years.

H. R. (C. H. No. 75329, case previously reported) female, was born June 12, 1924, and was first admitted to the hospital on Feb. 12, 1927. She had umbilical infection and general sepsis at birth. During the first year of life she was admitted to the Infants' Hospital several times because of gastrointestinal disturbances. At each admission she showed a secondary anemia. At one year of age the spleen was palpable 3 cm. below the costal margin. Two days previous to the first admission to the Children's Hospital, when two years and nine months old, she suddenly vomited a large amount of blood and was brought to the hospital in marked prostra-

tion. The spleen was not palpable. The platelet count was low. After transfusion the spleen increased in size to 5 cm. below the costal margin. One month after entry splenectomy was done by Dr. W. E. Ladd. No abnormalities or thromboses of the veins of the portal system or interference with the splenic circulation could be demonstrated at the time of operation. There were a few vascular adhesions between the upper pole of the spleen and the diaphragm. The spleen showed fibrosis. She had a recurrence of hemorrhage five months ago, eight years after splenectomy, and is in good condition at the present time.*

Fig. 1.—Case 4. Collateral circulation. Dilatation of superficial veins.

CASE 4.—Several infectious diseases, epistaxis, hematemesis at two and one-half years of age, spleen palpable, recovery, spleen increased in size, tarry stools, decrease in size of spleen, splenectomy, recurring thromboses, high platelet count, marked dilatation of superficial veins, fair condition.

G. S. (S. H. No. 102477, case previously reported), female, was born Aug. 15, 1924, and was first admitted to the hospital on Feb. 24, 1927. She had had measles, pertussis, chicken pox, and bronchitis. The mother stated that she had always been

*Since this was written she has had another hemorrhage from which she made a good recovery after transfusion. One month later Dr. W. E. Ladd tied the coronary vessels in the hope that further hemorrhage may be prevented. At operation the vessels at the cardiac end of the stomach were greatly dilated. The omentum was firmly adherent to the abdominal wall over a considerable area.

pale and occasionally had had nose bleeds. The day before entry, at two and one-half years of age, she complained of pain in the abdomen and vomited a large amount of dark, clotted blood. The spleen was palpable 3 cm. below the costal margin. She had no further bleeding and was not transfused. The spleen enlarged to 7 cm. below the costal margin. Without any subjective symptoms, while in the hospital, she passed tarry stools, and the spleen decreased slightly in size. Splenectomy was performed by Dr. W. E. Ladd six weeks after admission. At the time of operation the spleen was bound to the stomach at its upper pole by firm adhesions which bled easily, and in these adhesions there were a few large veins. No thromboses or obstruction of the splenic circulation could be demonstrated. The spleen showed characteristic fibrosis. She has had no further hemorrhages. Since July, 1929, she has had repeated attacks of severe abdominal pain and has been admitted to the hospital twice where presumptive diagnoses of mesentery thrombosis have been made. The possibility of intestinal obstruction due to adhesions was considered also, but gastrointestinal barium series were negative. Her platelet count since operation has been consistently high ranging from 310,000 to 1,220,000, usually above 500,000. In December, 1934, she had pneumonia. At that time the liver edge was palpable 2 cm. below the costal margin. Now at the age of ten and one-half years she shows marked dilatation of the superficial vessels of the chest and abdomen (Fig. 1), and her general condition is only fairly good.

CASE 5.—Normal infancy, measles, hematemesis at five years and nine months of age, epistaxis, recurrent hemorrhage, enlarged spleen, splenectomy, recurrent hemorrhages, tarry stools, intestinal obstruction, operation, good condition.

S. B. (private record, case previously reported), male, was born Feb. 9, 1917, and was first seen on June 3, 1924. His infancy was normal. He had measles at four years of age. In November, 1922, without warning, he vomited a large amount of bright and clotted blood. Fourteen months later he had severe epistaxis and another hematemesis. His condition at this time was critical. After recovery the spleen was found to be enlarged. He was seen five months later. On physical examination there was nothing remarkable except a large spleen which extended to the umbilicus and well into the flank. At seven and one-half years of age splenectomy was performed by Dr. Beth Vincent. No obstruction of the splenic or portal circulation was observed at the time of operation. The spleen showed characteristic fibrosis. Thirteen months later there was a slight gastric hemorrhage following severe physical strain. Two and one-half years after that he passed tarry stools for about two days. There was no abdominal pain or other subjective symptoms. He was well for over four years. Then tarry stools were noted again, and in a few days there was vomiting of bright blood. Moderate bleeding continued for several days. Convalescence was slow. Eight months later he vomited about a pint of bright red blood. This was not preceded by abdominal pain or other symptoms. He vomited again the next day, a much larger amount. A few days later he began to complain of severe abdominal pain. He developed definite intestinal obstruction which required operative intervention. The lumen of the intestine was found constricted by massive adhesions. A lateral anastomosis was performed by Dr. W. E. Ladd. Convalescence was stormy, but since then, for a year and one-half, he has had no further symptoms and no bleeding. His condition is good.

CASE 6.—Infection of leg at two weeks, convulsions at three months, hemiplegia at eighteen months, tonsillectomy at four years, hematemesis, recurrence, death from hemorrhage.

L. M. (C. H. No. 24601), male, born Jan. 31, 1920, was first admitted to the Children's Hospital when he was two weeks old because of an infection of the left leg. At three months of age he had generalized convulsions of unknown etiology lasting about a week. At eighteen months of age he was seen at the Children's

Hospital for hemiplegia which was attributed to a right cerebral hemorrhage. At four years of age his tonsils and adenoids were removed. Two days after the operation he vomited a large amount of bright blood. He was in the hospital for about two weeks at that time and was seen several times in the Out-Patient Department. Following the tonsillectomy, the spleen was not palpable or at a subsequent examination three weeks later. He had another period of vomiting within a few months, and at the time of discharge from that admission there was no mention of an enlarged spleen. The correct diagnosis was not made at this time. In 1930, at the age of ten years, he had severe hematemesis and was admitted to the Beth Israel Hospital. Through the kindness of the visiting staff of that hospital, he was seen in consultation. He obviously fell into the group previously reported. He continued to vomit large amounts of blood and died despite treatment. At necropsy "there was no gross evidence of obstruction of the portal vein or in the vascular supply around the celiac axis." The spleen showed characteristic fibrosis. There were marked varicosities of the esophageal veins. The details of the history during the last hospitalization and the necropsy findings are contained in a report by Fried.[9]

CASE 7.—Normal infancy, epistaxis and hematemesis at four years of age, spleen not felt, low platelets, recovery, spleen palpable, recurrent hemorrhages, low platelets, splenectomy, well for five years.

D. L. (C. H. No. 71178), male, born July 29, 1920, was first admitted to the Children's Hospital on June 2, 1924. Infancy was normal except for a questionable history of nasal diphtheria. No previous illnesses. At four years of age, one week before admission, there had been slight epistaxis and three days before severe hematemesis, which recurred several times up to entrance into the hospital. On the first physical examination the spleen was not palpable, and there were no striking findings except pallor and secondary anemia with low platelet count. He remained in the hospital for three weeks and was discharged in good condition. The spleen was palpable. There were recurrences of severe hematemesis two, four, and five years later. He was readmitted to the hospital during the last attack, and the spleen was removed by Dr. W. E. Ladd. It showed splenomegaly and fibrosis. He had a slow convalescence but was discharged in good condition. He remained well for five years up to Oct. 5, 1934, the time of the last report.

CASE 8.—Normal infancy, pertussis, epistaxis, hematemesis at eight years of age, spleen not felt, recurrences of hemorrhage, dilatation of superficial veins, normal platelets, spleen palpable, splenectomy, ligation of vessels, well for three years.

L. M. (C. H. No. 80942), male, born Feb. 13, 1917, was first admitted to the Children's Hospital on March 26, 1925. He was a normal infant. He had whooping cough at one year of age and for some time after that had epistaxis about once a month. Two days before admission to the hospital, at eight years of age, he complained of abdominal pain and the next day vomited bright blood. Vomiting of bright and clotted blood also occurred on the date of entrance. At that time his spleen was not palpable. He made an uneventful convalescence. Two and a quarter years later he had a second hematemesis preceded by abdominal pain. At that time the spleen was not felt on the first examination, but there was marked dilatation of the superficial veins of the abdomen. The platelets were normal. The next day the spleen was palpable and gradually increased in size to 4 cm. below the costal margin. He was discharged in good condition. Two years later he had another severe hemorrhage and was admitted to the Massachusetts General Hospital. Through the courtesy of the staff he was seen there in consultation. His spleen was removed by Dr. Arthur W. Allen, and a year later, because of the continued presence of dilated veins in the esophagus as demonstrated by direct examination, the vessels in the gastrohepatic omentum from the cardiac to the pyloric end of the stomach were ligated. Many adhesions were found at that time. He had one slight

hematemesis fifteen months later, but for the last three years he has been well and is in excellent condition at the present time.

CASE 9.—Diarrhea and bronchitis at nine months, spleen palpable at four years, hematemesis at nine years of age, decrease in size of spleen, low platelet count, splenectomy, death from pneumonia (embolism?).

L. C. (C. H. No. 65907), male, born March 5, 1923, was first admitted to the Children's Hospital on Jan. 26, 1931. He was seen in the Out-Patient Department of the hospital at the age of nine months because of "summer diarrhea" and bronchitis. At that time the spleen was not felt. At four and one-half years of age he was seen for abdominal pain with occasional vomiting. The spleen was just palpable. On admission to the hospital, at nine years of age, he gave a history of headache, fever, and vomiting of bright, red blood of one day's duration. He also had passed several tarry stools. The tip of the spleen was just palpable. The platelet count was low. The vomiting continued for several days, and the abdomen enlarged and showed free fluid in the peritoneal cavity. The spleen could not be felt. Splenectomy was done two weeks after admission by Dr. W. E. Ladd. The abdominal cavity was full of fluid. The spleen was much enlarged, and microscopic examination showed characteristic fibrosis. The day following operation the respirations became rapid and difficult, and there were signs of almost complete consolidation of the lower lobe of the left lung. He died very suddenly the next day. No autopsy was obtained. Death may have been due to pulmonary embolism.

CASE 10.—Difficult feeding history, several infectious diseases, hematemesis at eight and one-half years of age, spleen not felt, low platelets, recovery, spleen palpable, recurrent hemorrhages, splenectomy and ligation coronary veins, no hemorrhage for three months.

M. L. (C. H. No. 153653), female, born May 1, 1923, was first admitted to the Children's Hospital on Oct. 8, 1931. Infancy was normal except that there was considerable difficulty in feeding during the first few months. She had had measles, chickenpox, and pertussis. Two days before entry, at eight and one-half years of age, she complained of dizziness and the next day had pain in the chest and abdomen and felt nauseated. Two hours before admission she awoke from sleep with pain in the abdomen and vomited a quart of dark clotted blood. There were three or four similar vomiting attacks, the blood becoming brighter and more fluid. Examination showed nothing abnormal except pallor, rapid respirations, and shock. The platelet count was low. The bleeding subsided, and five days later the spleen was felt and increased in size during the next five days to 4 cm. below the costal margin. She was discharged at the end of five weeks when the spleen extended below the umbilicus. Esophagoscopy at this time showed slightly engorged minute vessels at the cardiac end of the stomach, but no varices or ulcerations were seen. She was readmitted one year later for a recurrence of hematemesis. Again the spleen was not palpable until after transfusion on the second day. The third admission occurred three months later on Dec. 22, 1932, and the fourth and fifth admissions on Jan. 7 and Jan. 20, 1934. At this time she had severe abdominal pain with extreme tenderness and spasm from the umbilicus to the right lower quadrant. It was felt that an extension of the thrombosis might have occurred although the number of blood platelets were not increased. She had a mild hematemesis, a period when she passed bloody stools, a severe hematemesis, and then another with a short stay in the hospital. There was another hospital admission one year later. Splenectomy with ligation of two coronary veins was done at the end of a week by Dr. W. E. Ladd. There were several large lymphatic glands along the course of the splenic vessels which were also removed. The spleen showed characteristic fibrosis. Convalescence from the operation was rapid. She had a gastrointestinal disturbance one month later with violent vomiting but no bleeding. She has been well for the last two months and is in good condition.

CASE 11.—Normal infancy, measles and pertussis, hematemesis at eight years of age, spleen not felt, transfusion, spleen palpable, recurrent hemorrhages, death from hemorrhage.

J. T. (C. H. No. 158802), male, born January 28, 1924. First seen at the Children's Hospital on March 29, 1932. Infancy was normal. He had had measles and whooping cough. At eight years of age, having previously been well, he complained of slight abdominal pain. The pain recurred six days later followed by the vomiting of a large amount of bright and dark blood. Hematemesis continued for the next two days. He was admitted to another hospital three days later. At entrance he was pale. The spleen could not be felt but after transfusion was palpable four fingerbreaths below the costal margin. When seen for the first time at the Children's Hospital, two months later, he presented nothing unusual on physical

Fig. 2.—Case 12. Esophageal varices.

examination except pallor. The liver could be felt three fingerbreadths and the spleen two fingerbreadths below the costal margin. His blood was normal except for 15 per cent eosinophiles. The platelet count was low. He was well for one month, then had severe abdominal pain followed by tarry stools, but no vomiting. Physical examination, three months later, showed the liver palpable three fingerbreadths and the spleen one fingerbreadth below the costal margin. During the next eighteen months he remained well except for occasional tarry stools. The liver and spleen both remained palpable. On Aug. 5, 1933, he had a sudden severe hematemesis, and despite transfusions he died three days later. No autopsy was obtained.

CASE 12.—Pertussis at fifteen months, hematemesis at sixteen months of age, low platelets, splenectomy and ligation of one vein, dilatation superficial veins, recurrent hemorrhage, death.

S. D. (C. H. No. 17867), female, born Dec. 26, 1930, was first admitted to the Infants' Hospital on May 31, 1932. She had whooping cough in March, 1932. In April, 1932, she vomited two or three "cupfuls" of blood. Six weeks later it was noticed that the abdomen had increased in size. At the time of admission, one week later, the spleen was palpable three fingerbreadths below the costal margin. The blood platelet count was low. Her condition was not very satisfactory, and during the period of observation in the hospital she vomited about 8 ounces of bright blood. Hematemesis of about the same amount occurred again four days later. Both of these attacks of vomiting were preceded by a slight rise in temperature. Because of the child's characteristic appearance, the roentgen ray findings, and consistent blood sugar curves, a tentative diagnosis of celiac disease was made in addition to splenomegaly. Three months later splenectomy was performed by Dr. W. E. Ladd, and a dilated vein at the cardia tied. The spleen showed splenomegaly and fibrosis. Following the operation she had tarry stools for a time and one month later vomited about eight ounces of bright blood. Two months after the operation she presented marked dilatation of the superficial veins of the chest and abdominal wall. Throughout her periods of observation in the hospital the number of blood platelets was low,

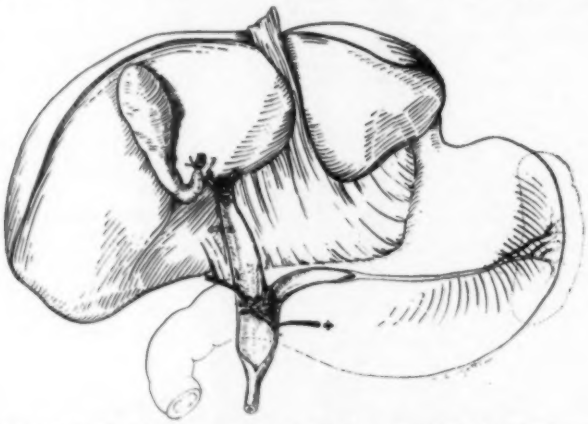

Fig. 3.—Case 12. Valves in portal vein. Canalized thrombosis forming membrane at junction of splenic, superior mesenteric, and portal veins.

usually below 200,000. She did well for one year at the end of which time she vomited two "cupfuls" of dark, clotted blood. This continued for two days, and despite transfusions she died. Necropsy was obtained. A summary of the pertinent findings follows.

The spleen had been removed about thirteen months before death. The lower end of the esophagus was the seat of marked changes in the submucosal veins which were greatly dilated and stood out clearly as long parallel cords (Fig. 2). The stomach contained about 20 c.c. of dark red bloody fluid. The mucosa was red and congested, but no definite ruptured veins or sources of bleeding were found. The small intestines were filled with frothy coffee-colored fluid material. Submucosal vessels stood out prominently throughout the entire bowel. The colon and rectum contained large amounts of dark red, bloody fluid mixed with fecal material. The inferior vena cava contained no thrombi. At the junction of the superior mesenteric vein, the splenic vein, and the portal vein, a membrane perforated by a large number of tiny openings formed a partial obstruction across the lowest part of the portal vein. The fenestrated structure was grayish white, firm and fibrous in consistency, and appeared to have a definite endothelial lining (Fig. 3). No fresh thrombi were

present in the portal vein or any of its tributaries. The membranous structure caused partial obstruction to the splenic vein and to the superior mesenteric vein. This structure probably represented the end-result of the repair of an organized and canalized thrombus. Just below the point of bifurcation of the portal vein at the hilus of the liver were found two small delicate valvelike membranes which stretched from one wall to the opposite wall without completely occluding the lumen. These had the appearance and position of congenital valves in the portal vein (Fig. 3). On microscopic examination of the liver revealed no periportal fibrosis.

CASE 13.—Normal infancy, several infectious diseases, hematemesis at nine years of age, recovery, increase in size of spleen, hematemesis later, convalescing.

V. P., female (seen in consultation with Dr. J. H. Young at the Cambridge Hospital), was admitted to the hospital on March 4, 1934, at the age of nine years. She had had measles, mumps, and whooping cough. The mother stated that she had always been pale. There was no history of previous vomiting or tarry stools. Six hours before admission, on waking in the morning, she felt dizzy and immediately vomited a "small dishful" of bright blood. She had five other hemorrhages during the next forty-eight hours. On the first examination the spleen was palpable 1 cm. below the costal margin. The white blood count was 17,000. The red blood cells showed normal fragility. The bleeding and clotting times were normal. Three days later the spleen had increased to 6 cm. below the costal margin. The liver was not palpable. The spleen remained at this size until discharge three weeks later. She had another hematemesis fourteen months later from which she was convalescing at the time this report was written. The spleen was to be removed and the vessels ligated as soon as possible.

CASE 14.—Abscess of leg at three months, several infectious diseases, hematemesis at the age of three years and eight months, low platelet count, transfusion, increase in size of spleen, splenectomy, hematuria, recurrent hemorrhage ten years after operation (one month before this report).

E. W. (C. H. No. 18864), male, born May 5, 1921, was first admitted to the Children's Hospital on Jan. 26, 1925. He was normal during infancy except that at three months of age he had an abscess requiring drainage below the left nipple. At one year and at two and one-half years of age he had otitis media, and at two years measles and chickenpox. For the last few years his family thought he was pale, and one year before admission the abdomen was noted to be prominent. Three days before admission, after a restless night, he vomited dark and clotted blood. Examination showed nothing remarkable except an enlarged spleen and a secondary anemia. The white blood count was 4,200, and the blood platelets were reduced in number. He had no further vomiting but passed tarry stools. His anemia increased. He was transfused on the fifth day in the hospital after which his spleen increased in size. His general condition improved. After a second transfusion the spleen was removed by Dr. W. E. Ladd. Convalescence was uneventful. The spleen showed characteristic fibrosis. The platelets were markedly increased immediately after operation but quickly returned to normal. The white blood cells rose to above normal. He had slight hematuria four years later. Otherwise he remained in good condition until April 1, 1935, ten years after the splenectomy, when, following a slight respiratory infection, he had a severe hematemesis. He was admitted to the Massachusetts General Hospital where through the courtesy of the staff he was seen in consultation. He made a good recovery after several transfusions. It was planned to ligate some of the veins going to the stomach and esophagus.*

*Since this report was presented, he suddenly developed severe pain in the abdomen, followed by abdominal distention, hematemesis, and death. Necropsy showed extensive thromboses and gangrene of a portion of the small intestine with perforation.

CASE 15.—Postnatal infection, "pyelitis" at four weeks, measles, abscess of jaw, abdominal distension, enlarged spleen, splenectomy, high platelet count, death from hemorrhage and extensive thrombosis at six and one-half years.

M. B. (C. H. No. 123133), female, born May 9, 1922, was first admitted to the Children's Hospital on Dec. 14, 1928. She had a questionable postnatal infection with generalized erythema but no fever. At four weeks of age she had malaise, hematuria, and vomiting which was diagnosed as "pyelitis." She had bronchitis at two years of age associated with measles but no other diseases. On Dec. 4, 1928, an "abscess in the left jaw" was drained. Following this the abdomen, which had always been large, suddenly increased in size. She came to the hospital for this abdominal distention. Physical examination showed a healed abscess of the jaw, one carious tooth, ascites, and an enlarged spleen reaching to the level of the umbilicus. The superficial veins over the abdomen were markedly enlarged. She was pale and the blood showed a secondary anemia with a white count of 4,000. The bleeding and clotting time and the fragility test were normal. The platelet count was low. Tuberculin and Wassermann tests were negative. The fluid in the peritoneal cavity rapidly decreased in amount. Splenectomy was performed on Dec. 28, 1928, by Dr. W. E. Ladd. There were many adhesions on the posterior border of the spleen. The spleen showed the characteristic fibrosis. She had a stormy convalescence from the operation but was discharged in good condition. The blood platelet count remained high—360,000 to 500,000, over 1,000,000 at one examination. She was readmitted one month later. Six hours previously, on waking in the morning, she felt nauseated and vomited "about a pint" of blood with some clots. She vomited three times again, but each time the amount of blood was less. Vomiting continued in the hospital, and she died on the second day. Necropsy was obtained.

A complete postmortem examination was performed. Only those findings bearing on the problem at hand are given. At the lower end of the esophagus one large tortuous vein was present beneath the mucosa. No varices were seen in the region of the cardia. The stomach was filled with a large amount of coffee-ground material. Large clots of blood, reaching 3 by 2 by 2 cm. in greatest measurements, were found in the stomach contents. In the distal portion of the jejunum and increasing in amount as the large bowel was reached, a fairly large amount of fresh blood mixed with fecal material was found. No single large point of rupture of a vessel could be recognized. Dissection of the portal vein and its tributaries disclosed thrombi which almost entirely filled the lumina of the vessels. The thrombus in the main portal vein appeared to be completely organized; those in the mesenteric branches of the portal vein, and in the splenic vein were of more recent formation. On microscopic examination of the portal vein, a completely organized and recanalized thrombus was found. Microscopic examination of the liver disclosed a moderate degree of fibrosis in the periportal areas accompanied by a moderate inflammatory reaction in those regions. The ramifications of the portal vein within the liver showed organization of old thrombi.

PATHOLOGY

The early writers who dealt with this subject believed that enlargement of the spleen was a primary pathologic condition brought about by the action of some toxin either generated within the spleen or absorbed from the intestinal tract. They believed that all other abnormal findings were secondary to the splenic dysfunction. Dock and Warthin[10] were the first to suggest that the splenomegaly was caused by an obstruction to the portal circulation as a result of thrombophlebitis. They believed that the changes in the spleen were

caused by chronic passive congestion and that all variations of the disease picture commonly called Banti's disease could be explained on this basis. Since the appearance of their publication there has been much discussion of the relationship between thrombophlebitis of the portal vein and splenic anemia and Banti's disease.[11] Warthin[12] later amplified his earlier observations and maintained that splenic anemia and Banti's disease did not represent disease entities. He stated that his conception must be accepted until it has been definitely shown that these disease complexes exist without evidence of obstruction in the portal or splenic vein. Although Warthin's view is not universally accepted, we believe that it offers an adequate explanation for the syndrome represented by the group of cases which we are reporting. Whether there is the same underlying mechanism in all cases of splenic anemia and Banti's disease is a question beyond the scope of this paper.

A large amount of literature has accumulated in support of Warthin's observations of portal or splenic vein obstruction. Wallgren[13] reported five cases identical with our group and discussed others from the literature. On the basis of necropsy findings he concluded that obstruction to the splenic vein was the causative factor. Wilson and Lederer[14] described in detail the pathologic changes in one case. They described the narrowing of the portal vein with changes characteristic of phlebosclerosis. In a recent discussion of this subject, Mallory[15] stated that his own experience has led him to follow Warthin in assuming a causal relationship between thrombosis of the splenic vein and splenomegaly of this type. Other reports in the literature give confirmation to the hypothesis of obstruction as the primary lesion. Proof of obstruction is lacking in most instances in which the evidence depends upon the examination of the vessels comprising the portal system made at the time of operative removal of the spleen. This, however, is not necessarily an indication that the vessels in such cases were normal, for investigation at that time is difficult and of necessity not exhaustive. How easy it is to miss, even at necropsy, an important involvement of the vessels in the portal system is shown by an experience reported by Mallory[15] who discovered a completely organized and partially recanalized thrombus in the splenic vein only by cutting a number of sections through the region of the pedicle of the spleen. Unless careful search is made in every case for evidence of obstruction in the portal or splenic veins necropsy findings are necessarily inconclusive. Warthin[12] called attention to the fact that the portal and splenic veins receive little attention in the usual necropsy. Despite the lack of confirmation in every instance, we believe that positive evidence of obstruction found in so many nec-

ropsies furnishes an adequate basis for assuming that obstruction was probably present in many others.

Macroscopic and microscopic study of the spleens removed at operation or at necropsy in this series of patients show findings consistent with the hypothesis that the changes are due to chronic passive congestion. The thickening of the capsule, the dilatation of the sinuses, and the diffuse thickening of the fibrous frame work of the spleen are all findings which occur in chronic passive congestion.

The spleens varied in weight from 65 to 530 gm. The majority weighed in the neighborhood of 250 gm. In general, essentially the same pathologic changes were found in all the spleens in this series. Variations in the pathologic picture were present, but these were dependent mainly upon the duration of the disease process. The usual findings in the spleen were as follows: The spleen is grossly enlarged and the external surface is mottled purplish gray in color. The capsule is thickened and tabs of adhesions are present over the surfaces of the upper pole. The borders are well rounded. The spleen is extremely firm in consistency and when sectioned the edges of the surfaces made by cutting do not evert. Such surfaces vary from gray to red in color and have a distinctly beefy appearance. The presence of a large amount of fibrous tissue throughout the organ is evident from gross appearance and palpation. The trabeculae are unusually well defined. The malpighian corpuscles do not stand out clearly. Very little blood appears on the surfaces made by cutting, and no pulp can be scraped by the knife edge. In those spleens which had reached a larger size numerous spots, averaging 1 mm. in diameter and varying from dark red to yellowish brown in color, may be seen on the cut surfaces. Small sections taken for microscopic study hold their shape well.

On microscopic examination the outstanding features are diffuse fibrosis, marked dilatation of the sinuses, hemorrhages in the zones about the malpighian corpuscles, thickening of the walls of the arterioles, and in some cases hyperplasia of the malpighian corpuscles. Hematopoiesis is sometimes present but never to a striking degree. The capsule and the trabeculae are prominent and possess increased amounts of connective tissue. Throughout the pulp there is diffuse and patchy fibrosis most marked in the subcapsular regions where both pulp and sinuses in some distances may be completely replaced. Hemorrhages may be found around the malpighian corpuscles, or perivascularly placed in the red pulp, or in the trabeculae. Both recent and old hemorrhages may be found. The older ones show organization and replacement by connective tissue which contains deposits of blood pigments. The sinuses are dilated, and the walls are thickened. The usual delicate reticulum is replaced in many areas by dense connective tissue containing many fibers having stain reactions characteristic of collagen. In the larger spleens in this series the pulp cords are obliterated by the fibrosis and the pressure of dilated sinuses. Frequently fibrosis appears to originate around the small arteries and to spread diffusely into the surrounding pulp with involvement of the pulp reticulum.

In addition to the diffuse fibrosis noted in the spleen by all observers, McNee[16] and later McMichael[17] have described progressive changes in the spleen. These consist of hemorrhage about the arterioles, followed by organization of the hemorrhages, during which process considerable amounts of hemosiderin are deposited. Small nodules of brownish fibrous tissue, called by McNee "siderotic nodules," are thus formed. The spleens in this series showed changes of this type. In the siderotic nodules, McMichael[17] found crystalline and amorphous iron pigments which consist of phosphate, carbonate, and probably also oxide and hydroxide of iron.

The nature of the obstruction to the splenic or portal vein may vary. Theoretically obstruction could be caused from pressure outside the vein or by pathologic changes of the wall or the lumen so that narrowing or partial obliteration of the lumen occurs.

1. Compression of the portal or splenic veins from without:
   a. Adhesions from repair of a previous peritonitis or from pancreatic fat necrosis
   b. A slowly growing tumor
   c. Gallstones
   d. Enlarged lymph nodes (tumor, chronic lymphadenitis).
2. Narrowing of the lumen of the portal or splenic vein:
   a. Phlebosclerosis caused by alterations in the pressure of the portal system (congenital?)
   b. Endophlebitis with stenosis (secondary to infection of umbilical vein)
   c. Thrombophlebitis (following damage to the veins in diseases of the gastrointestinal tract, or respiratory tract, in scarlet fever, in typhoid fever, in syphilis, or in pyogenic infections).
   d. Thrombosis of veins as a result of alterations in the composition of the blood
   e. Thrombosis following extension of thrombi from small veins within the spleen
   f. Thrombosis following damage to the intima caused by trauma(?).

1. Pressure on the splenic or portal vein from without, sufficient to cause obstruction, may occur from adhesions following previous local infection, such as peritonitis. We have had one example of such a change. In a necropsy on a four and one-half year old child, who had suffered from actinomycosis of the appendix with extension to the liver and peritoneal cavity, the portal vein, at a point just below the liver, was markedly compressed by dense adhesions. The splenic vein was dilated, and the spleen was greatly enlarged. It was more than six times the normal weight for this age. The capsule was thickened; the sinusoids were dilated; and diffuse fibrosis was present. The gross and microscopic changes in the spleen were identical with those found in the series reported here.

The frequent finding of enlarged lymph glands in the region of the splenic vein at operation and at necropsy has suggested possible pressure from this source. One of our patients (Case 10) showed many such enlarged glands. Hypertrophy of lymphoid tissue, however, takes place commonly in the presence of passive congestion. It is more likely that the enlargement of lymph glands is secondary in nature and does not antedate the splenomegaly. Warthin[12] and Sanford and Dolley[18] suggest that hyperplasia of lymph nodes is a compensatory phenomenon resulting from lost splenic function.

2. Obstruction within the splenic or portal vein may be due to persistence of fetal structures or to thrombophlebitis. In the fetus and for a short time after birth, valves are present in the portal vein and its tributaries. If these valves persist into late infancy and childhood, it is conceivable that interference with blood flow might result. In one of our patients (Case 12) two small valves, incompletely occluding the lumen, were found at necropsy in the upper portion of the portal vein. In this patient, however, a more severe obstruction, due to a canalized thrombus, was found at the junction of the portal and splenic veins. Valves were found also in infants dying of other conditions (Fig. 4).

In the great majority of instances it is probable that the cause of the obstruction to the return of blood from the spleen is thrombophlebitis of the splenic or portal vein. Canalization of the thrombus may take place, but the lumen of the vein will be narrowed.

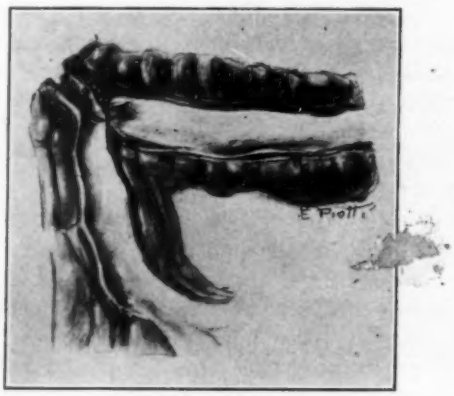

Fig. 4.—Valve in splenic vein.

Thrombosis may result from damage to the vein from trauma. We have not encountered this condition, but there are reports in the literature.[19]

Usually the thrombosis occurs secondary to infection in some other part of the body.

The source of infection may be in the gastrointestinal tract. One of our patients (Case 9) and a considerable number in the literature gave a history of bloody diarrhea in infancy.

Acute disease of the respiratory tract may be another source of thrombophlebitis of the portal vein. In 1920 one of us (R. M. S.) reported such a case with necropsy findings.[20] Mallory[15] refers to a patient who had portal thrombophlebitis following a respiratory tract infection with mastoiditis. Warthin[12] describes thrombophlebitis of the portal vein as a complication of pneumonia.

Infectious diseases of many varieties may be complicated by thrombosis. One of our patients (Case 2) had scarlet fever two years before the first hematemesis. After the scarlet fever the spleen was found to be enlarged. Other possible sources of infection may be mentioned, such as infections of the skin or osteomyelitis.

Wallgren[13] believes that infection of the umbilicus in the neonatal period is the primary focus in some instances. Kleinschmidt[21] also holds this opinion. They had no confirmatory evidence to support this hypothesis. One of our patients (Case 3) and possibly a second (Case 15) gave histories of omphalitis. We were able to study the distribution of infection in a number of infants dying of the consequences of umbilical infection. In these cases there was purulent endophlebitis involving the umbilical vein, the left branch of the

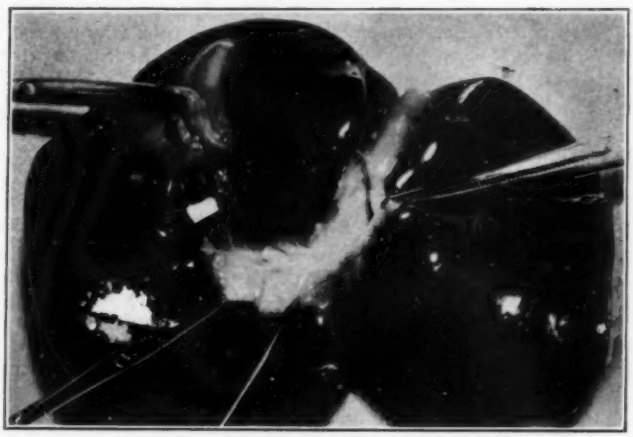

Fig. 5.—Omphalitis—showing pus in umbilical and portal veins.

portal vein, and the main portal vein as far as the splenic vein (Fig. 5). The spleen was enlarged to a size not found at this age (two to three weeks) following infection without portal vein involvement. The spleen on microscopic examination showed a marked degree of congestion and presented all the changes, except fibrosis, seen in the spleens described in this series. It is reasonable to suppose that in infants who survive, repair of such lesions in the veins might well lead to partial obstruction in the portal system.

RESULTS OF OBSTRUCTION TO THE PORTAL OR SPLENIC VEINS

As a result of obstruction to the flow of blood from the spleen, collateral circulation is established. The extent of the collateral circulation depends in part upon the location and the degree of obstruction. As pointed out by McIndoe,[22] the collateral channels develop

where contact between the portal and systemic circulation already exists. When the possibility of hemorrhage is considered, the most important location is where the coronary vein anastomoses with the azygos, intercostal and diaphragmatic veins at the cardia. It is in this region that esophageal and gastric varices are formed. By means of the gastrohepatic veins running along the greater curvature of the stomach, contact is established with veins on the surface of the body by adhesions between the omentum and the abdominal wall. The duodenal and left renal vein may also take some of the blood or blood may be carried through the accessory portal system of Sappey. A part of the blood may pass through the paraumbilical vein and cause the formation of the caput medusae in the region of the umbilicus. Blood may be diverted through the intestinal, inferior mesenteric, and hemorrhoidal veins, opening into the hypogastric veins.

A study of the circulation of the portal vein and its tributaries reveals the following possibilities. If obstruction occurs in the splenic vein the following circulatory changes, in addition to marked congestion of the spleen, may take place. Blood is backed into the short gastric veins following which dilatation of the underlying submucosal veins occurs. Because of the vast network of veins in and on the stomach, sufficient dilatation of the submucosal veins would, no doubt, be transmitted to other channels through which the blood would eventually lead to the portal vein above the obstruction. The return to the portal vein would very likely occur through the coronary veins and possibly through the pyloric and the right gastroepiploic veins. Because of the connection of the coronary veins with the esophageal veins, dilatation of the latter may well occur. In addition, there would be stasis in the inferior mesenteric vein, which would be forced to send blood by way of its superior hemorrhoidal branch to the middle and inferior hemorrhoidal branches of the hypogastric vein and into the superior mesenteric vein by way of the left colic branch. In all cases the amount of dilatation and varix formation would depend upon the amount of obstruction and the time over which the obstruction extended.

When obstruction occurs at the junction of the superior mesenteric and splenic veins, the problem is more complex, for the involvement of the gastroepiploic vein which now occurs results in increasing stasis in the veins of the stomach. The inferior mesenteric vein is also involved when the obstruction is located at this point. When the portal vein alone is obstructed, a different set of changes occur. The portal vein receives the superior mesenteric, the splenic, the cystic, the pyloric, and the coronary veins. In the fetus the umbilical vein empties into the left branch of the portal vein. Occasionally in the child or adult, paraumbilical veins may be found in the ligamentum teres of the liver and the middle umbilical ligament forming connections between the veins of the anterior abdominal wall with the portal, hypogastric, and iliac veins. When portal obstruction is present above the entrance of the splenic and superior mesenteric veins and below the entrance of the coronary veins, the problems are identical with those of combined superior mesenteric and splenic vein obstruction. When the obstruction in the portal vein is situated above the entrance of the coronary vein, large gastric and esophageal varices must inevitably occur.

Hemorrhage, which is such a prominent feature in this condition, is due to rupture of engorged veins in some portion of this collateral circulation. The commonest site of bleeding is the varices in the

lower end of the esophagus at the cardia. Melena is also frequent. There is often a history of repeated epistaxis and occasionally hematuria occurs (Case 14).

If such marked changes in the spleen as is seen in these cases is produced by chronic passive congestion, it is possible that other organs might also be similarly affected. If there is obstruction in the veins leading from the pancreas, changes could be produced which might lead to disturbance in function. Sanford and Dolley[18] report a patient with extensive thrombosis who showed at necropsy the tail of the pancreas very contracted and an increase in dense fibrous tissue. In all of our patients in whom a necropsy was performed the pancreas was normal.

TREATMENT

When a patient belonging to this group is admitted to the hospital with hematemesis, one is confronted with the treatment of an emergency. The measures to be employed depend upon a critical judgment of the exact condition of the particular child. The loss of blood has produced shock of varying degrees. One must decide whether the situation is so severe that a transfusion must be given at once in an effort to save life or whether the increase in blood volume and rise in blood pressure which follow the transfusion will induce further bleeding and hasten death. If possible, it is wiser to keep the patient quiet and allow the bleeding to subside before giving blood intravenously.

The question of further treatment after the bleeding has stopped presents real difficulties. If nothing is done, one can be almost certain that there will be recurrences of hematemesis and eventually one of them may prove fatal. Death has been due to uncontrollable hemorrhage in all of our fatal cases except two—one of which death resulted from postoperative pneumonia, possibly emboli in origin, and one in which hemorrhage was complicated by extensive thrombosis.* Reports of the favorable course of the disease are misleading because the intervals between hemorrhages may be long, often many years. These patients are always potentially in danger of sudden death despite their apparent good health.

Splenectomy has been employed in the treatment of Banti's disease and splenic anemia for many years. It seems a rational procedure because it removes from the portal system a large reservoir of blood and diminishes by at least 20 per cent the demand upon the dilated veins in the collateral circulation. It is possible that the dilated veins may become reduced in size, but there is no evidence that this occurs. Kirlin and Moersh[23] found no changes in the esophageal varices as

*See note on Case 14.

observed by roentgen ray nine days after splenectomy. Many of the early reports on the value of splenectomy are enthusiastic.[24] Osler[4] spoke of the results as brilliant. Pool and Shelman[25] said the effect upon the patient was "so striking that he seems to be cured." It does not, however, afford a completely favorable prognosis. It is well known that hematemesis occurs after splenectomy. Hanrahan[26] stressed this fact. There are other similar warnings in the literature.[27] In our experience recurrent hemorrhages after splenectomy have been common. Many of the favorable reports in the literature are not convincing because the patients have been followed for too short a time after the operation. In one of our patients a severe hemorrhage which nearly ended in death occurred nine years after the removal of the spleen. Another had no hemorrhage for ten years and then a very severe hematemesis.

Since hematemesis is not controlled by splenectomy alone, one must consider some further procedure. The bleeding is due to rupture of the dilated esophageal or gastric veins.* If the excessive flow of blood through these vessels could be controlled, some beneficial results might be expected to follow. Ligation of the coronary vein would reduce the blood going to this region and has been suggested by McIndoe[22] and others as a method of treatment. Walters[31] believes, however, that more than this should be done. Tying the vessels in the omentum along the curvature of the stomach would decrease the blood going to the stomach from that region. If adequate adhesions did not already exist between the omentum and the abdominal wall, collateral circulation via the superficial veins might be stimulated by an omentopexy as has been done in patients with cirrhosis of the liver.

In one of our patients (Case 8) Dr. Arthur W. Allen at the Massachusetts General Hospital, one year after a splenectomy, ligated the veins in the gastrohepatic omentum from the cardiac to the pyloric end of the stomach. One month later the dilated esophageal veins observed by esophagoscopy were definitely smaller than before the ligation. There was one slight hemorrhage sixteen months after the operation, but the patient has been well for three years and is in excellent condition. In our most recent splenectomy (Case 10) Dr. W. E. Ladd tied two branches of the coronary vein at the time that the spleen was removed. This was done too recently for the ultimate results to be known. It is of some interest, however, that one month after operation the patient had a digestive upset with severe vomiting and there was no bleeding. In one of our patients (Case 12) one large vein going to the stomach was ligated at the time of the

*These can be demonstrated by roentgen ray as described by R. Schatzki, Acta Radiology Supplement 18, 1933.

splenectomy, but she died one year later from massive hemorrhage. Greenwald[33] has recently reported a case in which the vessels going to the spleen and stomach were tied, but the spleen was not removed. The spleen which was palpable four fingerbreadths below the costal margin before operation was not palpable after the operation. This is also too recent a report to indicate ultimate results.

If the ligation of vessels proves to be a method by which hematemesis may be prevented, one might suggest a somewhat radical procedure at the time of a severe hemorrhage. If there is no tendency for spontaneous cessation of the bleeding and life is threatened, the coronary vessels might be tied after giving a large transfusion for immediate effect. If the operation itself did not cause too great shock, the bleeding might be controlled and recovery take place. This has never been done so far as we are aware, but, since many of these patients die of uncontrollable bleeding, it should be at least considered.

Splenectomy is not without operative risk. In other conditions in which this procedure is indicated the risk is not so great as to deter one from advising the operation. In this syndrome, however, there are two factors, hemorrhage and postoperative thrombosis, which considerably increase the hazard. There are always adhesions between the spleen and the surrounding structures, and these adhesions are very vascular. During removal of the spleen, excessive bleeding occurs. The immediate control of this may present real difficulty and the loss of blood adds to the shock of the operation. Thrombosis is always a possible postoperative complication of splenectomy. Since the underlying pathology of this disease is dependent upon thrombosis, an extension is particularly to be feared, especially into the mesenteric vessels. Emboli may be set free also into the general circulation.

It is important, if possible, to determine which cases are most liable to postoperative mesenteric thrombosis. There is considerable discussion of this subject in the literature especially by Rosenthal,[28] Klemperer,[29] and Evans.[30] If the blood platelets are normal or subnormal before operation, the outlook is usually favorable. In these patients there is a rise in the platelet count immediately after splenectomy, but by the end of the third week they return to normal values and remain so. In the group in which mesenteric thrombosis is more likely to occur the platelets are high or normal before operation but rise rapidly after splenectomy and remain permanently high. There may also be a shortening of the coagulation time.[30] One of our patients (Case 15) had postoperative thrombosis, and the number of platelets reached over one million. Another patient (Case 4) who has had attacks of fever and abdominal pain, considered to be due to

thrombosis, has shown consistently high blood platelet counts. They have never been below 300,000, usually between 430,000 and 650,000, and at one time reached 1,270,000. One must decide in the group with high platelet count whether the danger from postoperative thrombosis is so great as to contraindicate splenectomy. One might consider the possibility of treatment to reduce blood platelets after the spleen has been removed. There are several procedures which have been suggested to accomplish this, such as roentgen ray exposure of the long bones or administration of arsenic or some benzol compound. Cessation of treatment, however, is followed by a compensatory overproduction of platelets so that the beneficial effect could not be indefinitely obtained. Their use cannot be recommended.

Another late complication of splenectomy in these patients is intestinal obstruction due to adhesions. Hanrahan[26] reports one patient who died with this one year after operation, and one of our patients (Case 5), nine years after splenectomy, had an obstruction which was relieved only by operative interference.

Of the fifteen patients in this group, seven are dead. These all died of uncontrollable hemorrhage except one who had pneumonia. The hemorrhage in one case was complicated by extensive thrombosis. In three of the fatal cases the spleen had not been removed. Of those who are alive, eight in number, all but one have had splenectomy. One patient is just recovering from her second hematemesis and splenectomy will be done as soon as possible. In eleven of the fifteen patients the spleen was removed. There was one operative death due to pneumonia, possibly embolic in origin. One patient died six weeks after operation with extensive thromboses complicating hemorrhage. Two others died of uncontrollable hemorrhage. Seven are alive.* One was operated upon only three months ago. One has been well for five years since the operation. One has had multiple attacks of thromboses but no hematemesis. The remaining four have had recurrences of hemorrhage. One of these who had the vessels in the gastrohepatic omentum ligated had one slight hemorrhage two years later but has been well for three years. One has had multiple hemorrhages and intestinal obstruction. One had the first hemorrhage eight years after operation and one eleven years.

SUMMARY

We have reported observations on fifteen children with splenomegaly and early hematemesis.

These children present sufficiently characteristic findings to warrant their classification as a distinct clinical entity.

*One of these has died since this report was written (see Case 14).

Attention is called to the important significance of decrease in the size of the spleen after hemorrhage and the return to the previous or greater size after the restoration of blood loss.

The blood picture in this group is normal except immediately after hemorrhage when it shows a secondary anemia.

Children of this group have not developed cirrhosis of the liver and ascites as is characteristic in the late stages of Banti's disease.

TABLE II

CASE	AGE FIRST HEMATEMESIS	RECURRENCE OF HEMORRHAGE	SPLENECTOMY	RECURRENCE OF HEMORRHAGE	PRESENT CONDITION
1	5 7/12 yr.	Multiple (4)	No		Died at age of 12 10/12 yr. of hemorrhage
2	2 10/12 yr.	Multiple (2)	Yes at 3 9/12 yr.	Multiple (2)	Died at age of 4 2/12 yr. of hemorrhage
3	2 8/12 yr.	None	Yes at 2 9/12 yr.	Single*	Well. Age 10 11/12 yr. Hemorrhage five mo. ago
4	2 6/12 yr.	None	Yes at 2 8/12 yr.	None	Fair. Age 10 9/12 yr. Has had multiple thromboses
5	5 9/12 yr.	Single	Yes at 7 4/12 yr.	Multiple (3)	Well. Age 18 3/12 yr. No hemorrhage for 1 7/12 yr. Intestinal obstruction 9 4/12 yr. after splenectomy
6	4 yr.	Multiple (2)	No		Died at 10 yr. of hemorrhage
7	3 10/12 yr.	Multiple (3)	Yes at 9 1/12 yr.	None	Well. Age 14 9/12 yr. No hemorrhage for 5 yr.
8	8 1/12 yr.	Multiple (2)	Yes at 12 10/12 yr. Ligation of vessels 1 yr. later	Single (slight)	Well. Age 18 3/12 yr. No hemorrhage for 3 yr.
9	8 11/12 yr.	None	Yes at 8 11/12 yr.		Died of pneumonia (embolic?) postoperative
10	8 5/12 yr.	Multiple (8)	Yes at 11 9/12 yr. Also ligation of vessels	None	Well. Three months since operation
11	8 yr.	Multiple (2)	No		Died at 9 6/12 yr. of hemorrhage
12	1 4/12 yr.	Single	Yes at 1 7/12 yr. Also ligation of vein	Multiple (2)	Died at 2 9/12 yr. of hemorrhage
13	9 yr.	Single	No		Recovering from hemorrhage
14	3 5/12 yr.	None	Yes at 3 9/12 yr.	Multiple (2)	Recovering from hemorrhage†
15	No hematemesis before splenectomy		Yes at 6 7/12 yr.	Single	Died at 6 10/12 yr. from hemorrhage and multiple thromboses

*Another hemorrhage since report. See case history.

†Died at fourteen years of extensive thromboses, intestinal perforation, and hemorrhage.

The primary pathologic lesion is considered to be portal or splenic vein obstruction due, in most instances, to thrombophlebitis secondary to infection in some other part of the body.

Splenectomy does not prevent recurrence of hemorrhage. Ligation of vessels going to the stomach and esophagus offers a further means of treatment with the possibility of greater success in the prevention of recurrent hemorrhage.

A study of the blood platelet count gives some indication of the probability of postoperative mesenteric thrombosis.

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66 COMMONWEALTH AVENUE
THE CHILDREN'S HOSPITAL

MENINGOENCEPHALITIS FOLLOWING RUBELLA

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MY INABILITY to find meningoencephalitis reported as a complication of German measles prompts this report. It is common knowledge that meningoencephalitis may follow any infectious process, and the literature contains many reports of it as a complication of measles, mumps, and other contagious diseases. Its appearance, however, in such an innocuous disease as rubella, with resulting death in one case, warns against depreciating the potentialities in any minor illness.

During the months of December to February of this year, this community suffered a widespread epidemic of German measles. Unlike most epidemics, adults were afflicted as well as children. Since the disease in most instances was so mild that many people failed to report its presence, the actual extent of the disease during the epidemic remains unknown. At the onset of the epidemic the disease was mild, but as it increased the appearance of purpura and severe lymphadenitis became unusual complications.

CASE REPORT

J. S., white male, aged ten years, was seen at 9 A.M. on Jan. 25, 1935, at his home, and the following history was obtained. For the previous three weeks this child had been repeatedly exposed to German measles at school. He remained perfectly well, however, until Jan. 24, 1935, when he complained of a nasal discharge and felt feverish. His mother noted that his temperature was normal but that there was a definite swelling of the occipital glands. He felt perfectly well during that day, but, on awakening on the morning of January 25, he discovered he was covered with a rash. He felt perfectly well except for some pain in the enlarged occipital lymph nodes. The family history and past history are nonessential. Physical examination at this time revealed no evidence of any constitutional defect other than the present illness of German measles. His temperature was 99° F. His blood pressure was 118 systolic and 90 diastolic; the pulse rate was 90 per minute. The course of his illness was mild, and at no time did his temperature exceed 99° F. He felt so well on January 27 that his mother permitted him to ski down their front lawn. At noon of this day she called him into the house for dinner. The child washed himself and then began his meal. During the course of the meal the patient developed a speech defect which the family believed to be an assumed imitation of a popular radio comedian. However, as the meal progressed, it became apparent that the child had no control of his speech. When asking for meat, he said potatoes; and when asking for bread, he said cake. When the child was furnished with the meat he requested, he left the table, walked around it, and obtained the potatoes, which he actually wanted. As soon as this occurred, the father realized that the child was unable to express his wants, and, on questioning him as to the names of the foods on the table, he received incorrect names for each item of food.

From the Medical Service of St. John's Hospital.

The father obtained the impression that the child realized that his answers were wrong. I again saw the child at 2 P.M. on January 27, when he was lying in bed, apparently not acutely ill. His temperature was 98° F., and his pulse, 100 per minute. He answered questions unintelligently, and it was obvious that the child realized that these answers were wrong. Some of the questions revealed a very marked loss of memory for certain types of words. Physical examination revealed a lateral nystagmus. The pupils were widely dilated and reacted poorly to light. The fundus examination showed one diopter of papilledema. Further examination of the head showed nothing of note. Examination of the neck was completely negative, except for the enlarged occipital lymph nodes. Examination of the chest revealed no abnormality. Examination of the abdomen showed nothing of note. Examination of the skin showed that the rash was completely gone. Examination of the upper extremities revealed a definite paresis of the right arm associated with a slight increase of the reflexes of this arm. Examination of the abdominal reflexes revealed them to be markedly exaggerated. In the lower extremities the patellar reflex of the right leg was definitely increased, and on this side there were positive Babinski, Gordon, Chaddock, and Oppenheim reflexes. The left leg was practically normal as to reflexes. A definite ankle clonus existed in the right ankle. Kernig and Brudzinski reflexes were absent. A diagnosis was made of meningoencephalitis following rubella. When the child was about to be removed to the hospital, he was seized with a severe convulsion. After the convulsion subsided, exaggerated reflexes were obtainable in all members, and the left leg now displayed the same signs as the right leg. There also existed, at this time, an alternating spastic and flaccid paralysis. At the time of admission to the hospital, the patient was in extremis. His temperature gradually increased until it reached 107° F. by rectum, and definite pneumonia could be found in both lungs. Intravenous glucose was given, as well as morphine and chloral hydrate by rectum to control the convulsions. The convulsive seizures, however, were increasing in frequency, and despite all measures taken the child died of respiratory paralysis at 12:30 A.M. Jan. 28, 1935. A spinal fluid puncture was made by Dr. Hammes which revealed a clear fluid under marked pressure. The cell count was 51, with 98 per cent of the cells lymphocytes. The spinal sugar was 65 mg. per cent, and the blood Wassermann and spinal Wassermann tests were negative.

A postmortem examination was conducted by Dr. Noble, who reported as follows:

The body was that of a normally developed, well-nourished white male child measuring 42 cm. in length and weighing about 110 pounds. Postmortem rigidity was present, and there was a blotchy postmortem lividity over much of the body surface. There was no edema, cyanosis, or jaundice. The pupils were dilated, round, and equal. From the nose and mouth there was a dark bloody fluid exuding.

After the abdomen was opened, peritoneal surfaces were found to be smooth and shiny with no excess fluid present. The appendix was normal in appearance. The liver was flush with the costal margin.

When the thorax was opened, the lungs and the pleural cavity were found to be free, and the pleural cavities empty. The pericardial sac showed nothing of note. The examination of the large branches of the pulmonary artery showed no evidence of thrombi. The heart measured 9.5 cm. in width.

The heart weighed 190 gm. The coronary arteries were normal in appearance. The heart showed nothing of note. The myocardium on cut section was paler than normal and definitely swollen in appearance.

The left lung weighed 240 gm. and had three definite lobes. The pleural surface was smooth, and crepitation was slightly reduced throughout the lung. There were scattered small hemorrhagic areas of consolidation throughout the lung, particularly

in the lower lobe. The right lung weighed 305 gm. and showed a picture similar to the other organ, but here the areas of consolidation appeared more pronounced in the upper lobe.

The liver weighed 1,000 gm. The surfaces were smooth. On cut section the liver showed nothing of note, save for a moderate degree of cloudy swelling. The spleen weighed 94 gm. The organ was fairly firm, and the corpuscles were barely visible.

The right kidney weighed 80 gm. The capsule of the organ stripped easily, leaving the free surface. On cut section it showed nothing of note, save for a moderate degree of cloudy swelling. The left kidney weighed 85 gm. and showed a picture similar to the right.

Examination of the gastrointestinal tract showed nothing of note, save for the fact that the Peyer's patches were prominent and unusually dark in color.

The scalp and calvarium were found to be normal in appearance. Examination of the brain showed slight evidence of increased pressure with slight flattening of the convolutions. The brain on cut section showed scattered petechial hemorrhages throughout, most pronounced in the white substance in the base. The middle ears and mastoid processes showed nothing of note.

Diagnosis: (German measles). Postmeasles encephalitis. Bilateral hemorrhagic bronchopneumonia. Cloudy swelling of heart, liver, and kidneys.

On microscopic examination sections of the brain showed a definite perivascular infiltration of lymphocytes and polymorphonuclear leucocytes at many points. In certain areas the smaller vessels were also surrounded by collections of red blood cells. The splenic pulp contained many polymorphonculear leucocytes. The myocardium showed a moderate degree of cloudy swelling. The adrenals, liver, and pancreas showed nothing of note. Sections of the kidneys showed the glomeruli containing a considerable excess of nuclei, apparently due to a proliferation of endothelium. Sections of the lung showed many of the alveoli filled with blood, but very few inflammatory cells were seen.

CASE 2.—A boy, three years old, was first seen on Feb. 2, 1935. He was the youngest of six children, all of whom were suffering with German measles. The mother stated that the children had little difficulty with the disease and that for the most part they were up and around playing. The disease had made its appearance two days before, and nothing unusual was noted about it, until the morning of Feb. 2, 1935, when the patient refused to get out of bed. The mother paid little attention to this until noon, when she discovered, as she attempted to arouse the child from his sleep, that he was only partially conscious. I saw the child at 5 P.M. on that day, when the above history was obtained. His past history and family history are irrelevant.

Physical examination revealed a child covered with a characteristic rash of German measles. His temperature was 100° F.; his pulse was 130; and his respiration rate was 26 per minute. The scalp showed nothing of note. The eyes were fixed and staring, and the fundus was normal. There was no abnormality in the pupillary reflex. The eyes, ears, nose, and throat were normal. The occipital nodes were enlarged, but apparently not tender. The neck was normal. Examination of the chest revealed no pathology in the lung fields or the cardiovascular system. Examination of the abdomen showed nothing of note. The reflexes of the right leg were essentially normal. The left leg was spastic, and the patellar reflex was exaggerated. In the left leg there was a questionable Babinski reflex. Examination of the urine revealed a trace of albumin. The spinal fluid was under pressure, but clear. The cell count was 100 with 92 per cent of the cells lymphocytes. The spinal sugar was 70 mg. per cent.

A diagnosis was made of postrubella meningoencephalitis.

The child's condition did not seem serious, and on the next day there was a definite improvement. This improvement continued until, on Feb. 9, 1935, a complete physical examination revealed nothing abnormal. Shortly after this last examination, the family, who were transients, left the city, so that the present condition of the child is unknown.

In addition to the two cases reported above, I have knowledge of at least three other cases of meningoencephalitis occurring in this epidemic. All these patients recovered from the illness.

SUMMARY

Two cases of rubella are reported in which meningoencephalitis appeared as a complication. In one death ensued, and postmortem examination confirmed the clinical diagnosis.

It is suggested that meningoencephalitis is not an uncommon complication of rubella when the epidemic is severe.

706 Lowry Medical Arts Building

A CLINICAL EVALUATION OF SEVEN PRELACTEAL FEEDING PROCEDURES IN 962 CONSECUTIVE NEWBORN INFANTS

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THE newborn human is the only mammalian whose mother does not have a food supply ready for it at birth. From two to four days usually elapse before the mother's supply of milk appears. During this period, water and other foods have been supplied by the obstetrician and pediatrician. This interim supply has not always been satisfactory. When water alone is given, there may be fever and loss of weight. When a milk formula is given, the newborn infant may be so overfed that he is not hungry enough to relieve the engorged breasts when the mother's milk appears. If the mother has a sufficient milk supply for a long period, we may find later that the infant has been sensitized to cow's milk.

The recent studies of Eder and Bakewell[1] and Kugelmass[2] have focused new attention on prelacteal procedures. Evaluating their respective methods chiefly on the basis of reduction in the loss of birth weight, they have reported improvement over the results obtained by previous methods.

A brief review of the methods employed in these and previous studies may well preface an analysis of their results. Earlier studies on birth weight loss are mainly reports of averages among groups of infants fed the maternal colostrum supplemented by plain water. The weight losses range from 6.4 per cent for the infants of multiparas observed by Adair and Stewart[3] to 9.8 per cent, the figure reported by Herzfeld.[4] The average is about 9 per cent.

The rôle of colostrum in any prelacteal feeding will be referred to again later in this paper. We are convinced that any prelacteal feeding regimen which excludes the maternal colostrum when it is available or includes complementary formulas decided on without regard to the composition and physiologic functions of the colostrum is unthinkable, and furthermore we are convinced that complete, or nearly complete, breast feeding, when it is possible, is the method of choice.

To facilitate analysis, the prelacteal complementary foods reported in the literature and those in common use may be divided into three groups: Type I, the "complete" foods, containing proteins; Type II, simple carbohydrate solutions, and Type III, those of both preceding groups to which a salt has been added for extra hydrating value.

From the Kansas City General Hospital.

TYPE I

In the order of physiologic fitness, breast milk from foster mothers should rank first among all complementary foods for the prelacteal period. However, Eder and Bakewell,[1a] quoting Benestad, cite the failure of several attempts to lower loss in birth weight by placing newborn infants to the breasts of women whose babies had been born several days previously. It would seem that such milk of the transitional composition which still carries colostrum would be ideal for the purpose. Yet, Eder and Bakewell say, "Strangely enough in most of the cases studied, the loss of weight instead of being corrected was aggravated." As will be seen later, our own study showed little diminution in birth weight losses when expressed breast milk was used as the complementary feeding.

If breast milk has proved unsuccessful in reducing birth weight losses, it seems logical to ask if cow's milk, however modified, can be expected to do better. Experience as related in the literature indicates that cow's milk mixtures do not. Our own study also shows an almost negligible effect.

Regardless of their influence on birth weight loss, however, there is a far more important reason for avoiding cow's milk formulas in the possible danger of protein absorption. Placing responsibility for a large percentage of his marasmic cases on foreign proteins absorbed during the newborn period, Pritchard[5] states, "It is quite useless or even dangerous to supply the newborn infant with any variety of foreign proteid unless, or until, the digestive functions have been established." He says further, "Even the colostrum of a wet nurse does not contain proteins identical with those of the child's mother and wet-nursing should not be attempted during the first few days of life."

Although much about the subject is yet unknown, most authors believe that the intestinal tract of the newborn infant is more permeable to undigested protein than that of an older child. Schloss and Worthen[6] in 1916 agreed that there may be protein absorption among young infants when some abnormal or pathologic condition exists in the gastrointestinal wall. Ratner and Gruehl[7] have more recently demonstrated that, although pathologic conditions increase the intestinal permeability, protein absorption also occurs with great regularity when the intestinal mucosa is normal. Ratner and his associates[8] have also demonstrated that sensitization of the fetus can occur in utero.

Sensitization to proteins absorbed during the prelacteal period may never be precisely established because allergy is rarely demonstrable before an incubation period of three weeks or more. There always is difficulty in attributing allergic manifestations in infancy to

foods given during the prelacteal period until intrauterine sensitization can be excluded as the possible cause. However, with sensitization both in utero and in early infancy established, the certainty of its occurrence during the first seventy-two hours of life may be considered axiomatic. It is probable that sensitization is even more likely to develop at this time than in later infancy because of greater possible permeability of the intestinal tract of the newborn.

It would seem a safe conclusion that many of the allergic manifestations encountered in weaning are due to sensitization by needlessly fed prelacteal formulas containing antigenic protein. With breast milk assured on the fourth day for a majority of infants and with colostrum already supplying a high percentage of natural protein, the feeding of a cow's milk formula during this short prelacteal period seems not only futile but disturbing. Furthermore, the newborn infant may be so satiated with food he will not nurse the breasts of the mother when they become full and need to be relieved. When this engorgement exists, it frequently happens that the mother's fluids are restricted; then the milk supply decreases, perhaps permanently.

TYPE II

The simple sugar solution, usually of lactose, is perhaps the most widely used prelacteal complementary formula. The clinically noticeable improvement of babies on such a regimen is marked. Ample justification for the procedure is found in the studies on energy requirements of the newborn which prove the critical and immediate need for sugar after birth.

Hasselbalch, as quoted by Murlin,[9] found the respiratory quotient of infants very high immediately after birth. He attributes this to the stress of birth, which has caused the glycogen reserve of the liver to be emptied into the blood stream where it is rapidly burned. Morris[10] published sugar analyses of the maternal and umbilical blood, which showed that the blood sugar level is raised in both bloods by a severe labor or by the use of an anesthetic.

The abnormally high respiratory quotient immediately after birth falls rapidly toward the end of the first day. Bailey and Murlin[11] made observations on two infants who were born three hours apart on the same day and placed in the respiration incubator at the age of six hours. The observations were repeated on the second, fourth, fifth, and sixth days with one child, and on the second, fourth, fifth, and eighth days with the other. The quotient fell to 0.67 in both cases on the second day. While distrusting the exact figures obtained, these authors point out the significance of the indication, confirmed in a third newborn baby at the twenty-fourth hour, that all available carbohydrate had been utilized by this time, and they emphasize the

importance of supplying artificially, if need be, some material to protect the body substance. Murlin concludes, "Unless artificial feeding is resorted to, the modern infant is doomed to almost complete starvation for the first three days, although it is clear that glycogen is present in sufficient quantity to prevent starvation acidosis the first day."

There can be little doubt of the imperative need for sugar to save body tissue during the prelacteal period. That the newborn infant can metabolize sugar without difficulty has been repeatedly shown. Murlin says, "Studies by Hasselbalch indicate clearly that the infant at term, or even if born prematurely, is able at once to burn either grape sugar, milk sugar, or cane sugar."

In our study, except for a shift from the alpha to beta form of lactose because preliminary comparisons indicated that the latter was somewhat superior, no comparative study of the various sugars was attempted. The argument for lactose as the sugar of choice seemed impregnable. It was our experience that of the seven complementary foods tried, these two sugars in simple solution were surpassed in all round suitability as prelacteal foods only by the beta lactose solution with sodium citrate added.

TYPE III

In an effort to combat the fever of inanition and the correlated acidosis among newborn infants, Eder and Bakewell[1a] in 1931 added 5 grains of sodium citrate to each 2 ounces of a 5 per cent lactose solution fed during the prelacteal period. Regarding its effect, they say, "The decided improvement in the general condition of the infants, with the smaller initial loss in weight and the absence of the inanition temperature, icterus neonatorum, and vomiting, was at once apparent." In a second paper[1b] covering a total of 379 infants similarly fed, they report that the average initial loss of weight was 5 ounces, and that 82.55 per cent of the infants regained their birth weights by the fourteenth day. One important clinical observation was that infants fed the solution showed a "far better" ability to nurse.

Salts are markedly superior to sugars in their water-binding property. There can be little doubt that the decreased loss of birth weight and the accelerated return to birth weight observed in this study are largely attributable to the hydrating effect of the added salt. Eder's choice of sodium citrate, for his solution seems particularly apt because it combines with hydrating value a compensating effect on the acid-base balance which, because of starvation, so frequently tends toward acidosis in the newborn infant.

The prelacteal hydrating solution proposed by Kugelmass and his associates[2b] follows the Eder principle of combining a hydrating salt with sugar but departs from it with the addition of a protein (gela-

tin). His solution consists of 6 per cent gelatin, 3 per cent dextrose, and 0.5 per cent sodium chloride. A study of Kugelmass' report reveals that the unusually small loss of birth weight observed was not attributable to his hydrating solution per se. Rather, it was the result of a regimen that included doubled feeding and nursing care of such meticulousness that it warranted the term "psychologic conditioning." The fact that the conditioned infants had nearly double the fluid intake of those who were not conditioned shows that such conditioning was an important factor. The increased number of feedings plays an equally important part, as shown by the doubled weight loss when only six feedings of his solution were administered in twenty-four hours instead of the twelve called for in his recommended procedure. When the hydrating solution is considered per se, it seems that sodium citrate as used by Eder has, in its slight alkalinity, some advantage over the sodium chloride.

Kugelmass' use of gelatin is in accord with his previous work on the effect of high protein feeding on blood clotting function.[12] Gelatin undoubtedly has its place as an excellent supplementary protein in later infancy. Our results raise the question as to the advisability of its use in the newborn infant. It is significant that gastrointestinal upsets occurred more frequently in the gelatin-fed group in our study than in any other. As a possible consequence, a larger percentage of this group, as compared with all others, was either completely weaned or given complementary bottle feedings by the tenth day.

Neither Eder nor Kugelmass explained his choice of sugar. On this score certainly much can be said. Pritchard[5] refers to the first days of life as a period of necessary digestive education when the infant's gastrointestinal tract adjusts itself through "the gradual metamorphosis of its mother's colostrum into the ordinary milk of full lactation." This educative adaptation of the digestive processes may be inhibited by foods not in harmony with the components of breast milk. The theoretical reasons for choosing lactose in the later feeding perhaps do not apply in the selection of a carbohydrate for prelacteal complementary feeding. During this period when harmony between the breast milk and a complementary food is the paramount consideration, the selection of lactose seems imperative because of its identity with the carbohydrate in breast milk.

Kendall[14] in 1911 pointed out the ready assimilability of lactose and its effect on the intestinal flora. The recent work of Gerstley on the chemistry and bacteriology of the intestinal tract as affected by carbohydrates seems especially pertinent. Gerstley[13] has found that unnatural fecal flora and an intestinal reaction close to the alkaline follow the ingestion of vegetable sugars of the maltose-dextrin type when combined with cow's milk in the artificial feeding. When a

sufficiently high percentage of lactose is used, the gram-positive flora and definitely acid intestinal tract of the breast-fed infant are observed. For this reason, Gerstley questions the physiologic fitness of vegetable sugars for the infant condemned to artificial feeding. This question is very much more pertinent when applied to the newborn infant for whom any digestive disturbance may prove a bar to the uneventful acceptance of his mother's milk.

PLAN OF PROCEDURE

To determine the most satisfactory prelacteal regimen for routine use at the Kansas City General Hospital, seven different procedures were compared under identical routine conditions (with one exception as noted below). Of a total of 984 infants born during a fifteen-month period, 962 were included in the study. Premature infants and those weighing less than 5 pounds at birth were excluded, because the premature infant and the baby under 5 pounds at birth require individual consideration as far as foods and treatment are concerned.

All babies were put to the breast throughout the prelacteal period. The first feeding was given at the sixth hour, after which a four-hour schedule was maintained. One group received only water in addition to the maternal colostrum. Each of the six remaining groups received one of the complementary formulas described in Table I. These feedings were offered immediately after the infant was returned to the nursery from his mother's breast. Only the gelatin solution was again offered at the hour midway between feedings—the only departure from identical nursing care and routine throughout the study.

TABLE I

COMPLEMENTARY FEEDINGS USED AND FORMULAS

GROUP	COMPLEMENTARY FEEDING	STOCK FORMULA	AMOUNT OFFERED EACH FEEDING (OZ.)	NUMBER DAILY FEEDINGS
1	Water		2	6
2	Expressed breast milk		2	6
3	Half skim milk, water, and dextrimaltose	9 oz. ½ skim milk, 9 oz. water, 1 tbs. dextrimaltose	2	6
4	Alpha lactose (milk sugar)	Alpha lactose 2 oz. Boiled water, 32 oz.	2	6
5	Beta lactose	Beta lactose 2 oz. Boiled water, 32 oz.	2	6
6	Gelatin solution	Gelatin 6 tbs., dextrose 3 tbs., sodium chloride, 1 teaspoonful, water q.s. ad 32 oz.	2	12
7	Beta lactose and sodium citrate	Beta lactose 2 oz. Sodium citrate 1 dram Boiled water, 32 oz.	2	6

During the first four days infants were kept at the breast for three minutes. Small sand glasses were issued to mothers for the timing.

For the complementary feeding in the nursery, the infant was held in the nurse's arms. Bottles were not given to the babies in the cribs. To minimize any preference for the bottle, five minutes, seldom more, was allowed for this feeding. It should be emphasized that the cardinal aim of this study was to evaluate the prelacteal procedures under conditions of average hospital routine. There was no unusual effort to achieve the "serene adjustment" between infant and nurse advocated by Kugelmass.

The infants were weighed before and after nursing and again after the complementary feeding. (This we would hope to avoid in actual practice as not being essential in all cases.) The prelacteal complementary foods studied were fed from the sixth hour of life through the fourth day. Thereafter, breast-fed infants received only water or such supplementary formulas as were individually required. Each attending physician was permitted to use the method he preferred. The breast milk used was supplied by the hospital breast-milk station, which pools surplus milk from both lactating in-patients and approved out-patients.

Daily Intake.—The variations in the average daily intakes of the groups as shown in Table II indicate that the "acceptability" of the complementary food may be important.

TABLE II

AVERAGE DAILY INTAKE OF COMPLEMENTARY FOODS

GROUP	COMPLEMENTARY FOOD	TOTAL NO. OF INFANTS	TOTAL VOLUME OFFERED	AVERAGE TOTAL DAILY INTAKE		
				IN OUNCES	IN PER CENT OF BIRTH WEIGHT	IN CALORIES
1	Water	70	6×2 oz.	2.5	2.2	--
2	Breast milk	20	6×2 oz.	2.6	2.3	52
3	Skim milk and dextri-maltose	151	6×2 oz.	2.9	2.6	27
4	Alpha lactose solution	180	6×2 oz.	3.2	2.8	21.8
5	Beta lactose solution	55	6×2 oz.	3.5	3.1	23.8
6	Gelatin solution	235	12×2 oz.	4.9	4.4	59
7	Beta lactose—sodium citrate solution	251	6×2 oz.	4.2	3.8	28.6

There is, naturally, some correlation between the daily fluid intake and the relatively lower weight losses which are tabulated in Table III. It does not follow, however, that this correlation explains completely the better effects among the lower groups, as will be seen when the rates of recovery to birth weight are studied in the same table. The caloric value of the daily intake, also listed in Table III, had no apparent influence on the initial weight loss, the time of recovery to

birth weight, or the tendency to nurse. The only slightly greater daily intake of the gelatin group is distinctly surprising when it is considered that these infants were fed twice as often as the others. The figure is but one-quarter of that reported by Kugelmass. It is unfortunate that his paper does not give the length of the feeding periods so that further conclusions might be drawn. It is worthy of record that our gelatin-fed group, despite the short feeding period, regurgitated far more frequently than the infants in any other group.

Initial Weight Losses and Rate of Recovery.—Because of the better results with beta lactose shown in a comparison of Groups 4 and 5, it seemed evident that this type of milk sugar even in simple solution possesses some advantage over the alpha form. It was because of this apparent advantage that the beta form alone was used for the lactose–sodium citrate group.

TABLE III

EFFECTIVENESS OF PROCEDURE IN LOWERING LOSS OF BIRTH WEIGHT AND IN ACCELERATING RECOVERY OF BIRTH WEIGHT

GROUP	COMPLEMENTARY FOOD	TOTAL NO. OF INFANTS	AVERAGE BIRTH WEIGHT (IN LB.)	AVERAGE INITIAL LOSS		PERCENTAGE OF GROUP BACK TO BIRTH WEIGHT	
				OUNCES	PER CENT	ON FIFTH DAY	ON TENTH DAY
1	Water	70	7.12	9.3	8.2	5.7	26.6
2	Breast milk	20	7.08	8.3	7.3	12.5	47.7
3	One-half skim milk and dextrimaltose	151	7.25	8.7	7.5	13.3	57.1
4	Alpha lactose solution	180	7.00	6.5	5.8	12.0	51.2
5	Beta lactose solution	55	7.15	5.9	5.2	18.2	59.0
6	Gelatin solution	235	7.12	5.0	4.4	23.2	73.4
7	Beta lactose—sodium citrate solution	251	7.10	4.4	3.9	62.3	80.5

The beta lactose–sodium citrate solution proved most effective of all the foods used in decreasing initial birth weight loss, in speeding recovery to birth weight, and in conditioning infants for the breast. The results observed with this solution are the more remarkable when the adverse conditions prevailing during its most extensive use are considered. The formula was the only one employed through July, August, and September, 1934, when 198 babies of a total of 251 in the group were born. This was a summer of extended drought during which Kansas City suffered the highest temperatures and the most prolonged heat waves of its history.

The beta lactose–sodium citrate group showed an average birth weight loss of 3.9 per cent, or 4.4 ounces. In most cases the maximum loss was observed on the third day.

This low initial loss is overshadowed by the remarkably rapid weight recovery of this group, 62.3 per cent of whom regained their

birth weights by the fifth day. The data for this period much more clearly reflect the comparative effectiveness of the several procedures than the ten-day figures after six days of breast feeding.

The superior findings in Group 7 over the gelatin-fed group are particularly surprising when it is considered that the latter were fed twelve times daily. On no point of comparison do results with the gelatin feedings justify the extra burdens its use imposes on both infant and the nursery staff.

The simple solution of beta lactose proved superior to the cow's milk formula on every point; the alpha lactose was likewise superior to cow's milk except in its effect on weight recovery. In this respect the alpha lactose lagged slightly.

The cow's milk formula had an almost negligible effect on the prevention of weight loss; it did little better than plain water. Furthermore, except for the gelatin solution, it was the least well tolerated of all the foods, as well as least effective in conditioning infants for the breast.

The infants in Group 1, who received only water as a complement to the colostrum and might be termed the control, fared the worst. Temperatures among this group were consistently higher than among the others. Inanition fever, not observed in the other groups, developed in about 10 per cent of these babies. The group was apathetic and nursed less vigorously than the others. On the whole, our observations on this group left little doubt of the need for food in addition to fluid during the prelacteal period.

Effect of Procedures in Conditioning For or Against Successful Breast Feeding.—References have been made to the relative efficacy of the various foods in conditioning infants for (or against) breast feeding. These refer to the data in Table IV. Since this was not considered in our original plan, the possible value of these comparisons became apparent too late to permit the explicitly detailed study which the subject seems to warrant. The limited data submitted are offered chiefly in the hope that the significant implications will lead other investigators to cover the subject more fully.

A twofold purpose dictates the form of Table IV: First, it is intended to show how the various groups were dispersed over the trial period. The obvious impracticability, under hospital routine, of using the seven procedures simultaneously, made a less complicated arrangement imperative. Second, the table shows that as many as four procedures were in use at one time, from which it can be seen that staff and seasonal variations do not account for the widely dissimilar results observed.

One of the major justifications advanced for prelacteal feeding is

TABLE IV

PERCENTAGE OF EACH GROUP PARTLY OR WHOLLY ON ARTIFICIAL FEEDING AT TENTH DAY

MONTH	WATER	EXPRESSED BREAST MILK	SKIM MILK DEXTRIMALTOSE	ALPHA LACTOSE	BETA LACTOSE	GELATIN SOLUTION	BETA LACTOSE SOD. CIT.
October	8.7	5.0	–	3.3	–	9.0	–
November	6.9	–	–	5.0	–	12.0	–
December	7.1	–	–	5.0	–	9.1	–
January	–	–	–	2.0	–	19.4	–
February	–	–	–	3.3	–	17.7	–
March	–	–	–	3.3	–	18.7	–
April	–	–	17.1	–	–	–	–
May	–	–	5.6	–	–	–	–
June	–	–	12.3	–	–	–	–
July	–	–	–	–	–	–	3.2
August	–	–	–	–	–	–	3.2
September	–	–	–	–	–	–	2.7
October	–	–	–	–	0.0	12.5	0.0
November	–	–	–	–	5.5	10.5	0.0
December	–	–	–	–	5.0	22.2	5.2
Average for whole group	7.6	5.0	11.7	3.7	3.5	14.6	2.4

the belief that it conditions infants for more vigorous nursing. This assumption would seem to be confirmed by the findings in Groups 4, 5, and 7. Among these, the percentages of infants requiring either partial or complete artificial feeding by the tenth day are, respectively, 3.7 per cent, 3.5 per cent, and 2.4 per cent as compared with 7.6 per cent for the colostrum and water group. We are excluding the infants fed expressed breast milk from this consideration because of the possible error with a group so small. Quite different findings will be noted for Groups 3 and 6. Of these, 11.7 per cent and 14.6 per cent, respectively, were partly or wholly bottle fed by the tenth day.

The implications are interesting. That lactose solutions condition the infant for the breast seems apparent. Is it probable, on the other hand, that certain types of prelacteal foods exert an opposite effect? Is it perhaps because of digestive derangement or other cause brought about by some foods that the infant is unable to or refuses to nurse at the breast? Is it mere coincidence that the two foods which apparently militated against the breast supply are cow's milk and gelatin formulas, both of which contain foreign proteins; furthermore, that regurgitation and vomiting during our study were markedly greater with these than with the other foods? Have we kept a certain percentage of infants from breast feeding by administering, before their mothers' milk appeared, foods incompatible with the digestive pattern of the newborn?

SUMMARY

The methods commonly employed in the feeding of newborn infants are reviewed and discussed from the standpoint of their theoretical compliance with the requirements of the infant during this period.

Evidence is cited to demonstrate the need for carbohydrate shortly after birth. The effect of lactose on the flora and reaction of the intestine influenced its selection.

Salt intake is likewise held to be desirable because of the need for a hydrating agent. An alkaline salt is preferable because of the compensating effect on the acid-base balance.

In 962 cases, over a period of fifteen months, seven different complementary prelacteal feeding procedures were studied. The procedures were evaluated by comparing the initial weight loss, rapidity of recovery to birth weight, and the conditioning effect as reflected by the number in each group who were discharged nursing at the breast.

CONCLUSIONS

1. Breast milk from foster mothers as a prelacteal feeding was ineffective in reducing birth weight losses and accelerating recovery to birth weight.

2. It was impossible in a group of 235 infants fed a gelatin-dextrose-salt combination every two hours to confirm the results originally reported by Kugelmass. This group contained the greatest number requiring artificial feeding upon discharge.

3. A cow's milk formula was found ineffective in combating initial weight loss, was less well tolerated, and apparently militated against successful breast feeding. The antigenic properties of cow's milk protein are advanced as an additional objection to such formulas during the prelacteal stage.

4. Plain water or simple sugar solutions were effective, but less so than a solution beta lactose with sodium citrate. In the simple solutions, beta lactose was found more effective than alpha lactose.

5. The lowest average birth weight loss (4.4 ounces), as well as the greatest percentage (62.3 per cent) regaining birth weight on the fifth day or earlier, was obtained in the group given the beta lactose–sodium citrate solution.

6. The caloric intake on the various feedings was of no significance.

7. Compared with a group receiving only water in addition to colostrum, the three lactose groups were better conditioned for the breast as evidenced by smaller percentages requiring artificial feeding on discharge. This effect was most marked in the beta lactose—sodium citrate group in which only 2.4 per cent were either partially or wholly artificially fed by the tenth day. Fourteen and six-tenths per cent of the group given the gelatin-dextrose-saline mixture and

11.7 per cent of those given a 50 per cent dilution of half skim milk with dextrimaltose were artifically fed by the tenth day.

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CONGENITAL MUSCULAR DEFECTS

With Special Reference to Deficiencies of the Pectoral Muscles

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CONGENITAL muscular defects are not very rare and many examples are to be found in the anatomic literature. Most of them are not recognized during life, for often large deficiencies, which cause pronounced deformities, do not result in any particular functional disability and are called to our attention only by routine examination. Agenesis of individual muscles occurs more often than combined muscular defects, while bilateral symmetrical absence is so rare that only six cases are on record.[1]

Defects of the pectoral muscles, serratus anterior (magnus), quadriceps femoris, trapezius, extensor pellicis longus, abdominal muscles, deltoid, external eye muscles, and facial muscles have been described.[2] Clinical interest centers largely about the abdominal and pectoral abnormalities.

Those peculiar and rare instances of abdominal amyogenesis are particularly noteworthy, for if this defect be extensive it is incompatible with longevity. Thirty-four cases of congenital absence of the abdominal muscles have been reported.[3] The oblique muscles are most frequently involved while the recti are affected least. These cases often show genitourinary anomalies such as hypospadias, hypertrophy of the bladder wall, and undescended testicles. The etiology remains obscure although a large number of theories have been propounded, among which are intrauterine infection, toxemias, hereditary influences, syphilis, intrauterine pressure, and amniotic disturbances. The burden of evidence apparently points toward a mechanical causation from an excessively distended bladder in early embryonal life.[4] The condition is apparent at a glance owing to the wrinkled skin, which hangs in loose folds over the abdomen. Treatment consists in surgical amelioration of the accompanying genitourinary abnormalities.

While congenital absence of the pectoral muscles is the most frequent of the muscular defects, it is by no means a common clinical entity. Scheslinger encountered it but five times among 54,000 patients.[5] In 1902 Bing[6] collected a series of cases of amyogenesis and found that a loss of pectoralis major and minor together constituted the commonest anomaly, being 28 per cent of the total. The absence of the sternocostal portion of the pectoralis major alone was next in

frequency, comprising 9 per cent. In all probability these figures are relatively somewhat high as some of the other muscular defects require a more detailed examination for their elicitation and are likely to be overlooked. In 1923 Morley[7] reviewed the literature and found that there were then about 220 cases listed. Since that time twenty-six additional cases have been reported, bringing the total at present to about 246. A very great majority of these have been described in adults.

In considering pectoral variations, the muscle may be looked upon as composed of four portions—clavicular, sternal, costal, and abdominal, the last being that portion which arises from the aponeurosis of the external oblique.[8] These portions vary in the extent of their attachments and in the degree of separation which they present. The sternocostal portions of the muscle are more often deficient or missing than the clavicular, and in rare instances the entire muscle is absent. A complete unilateral absence of the pectoralis major and minor has been observed by four authors[9] while only two cases of complete bilateral absence could be found.[1b, c] Christopher,[10] in his review of the subject, could find no evidence that the pectoralis minor was absent without accompanying defects of the pectoralis major and concluded that it probably did not occur. However, in 1930 Williams[9b] contributed a most unusual case in which there was a complete absence of the left pectoralis minor with the pectoralis major muscle intact. The condition was discovered during a mastectomy, and he pointed out that the detection of a pectoralis minor variation by clinical observation is impossible in the presence of a normal and well-developed pectoralis major.

Recognition of the usual pectoral agenesias is without difficulty owing to the flat appearance of the infraclavicular region on the affected side. Defects in the nipple and mammary gland are frequently present; both may be completely absent,[11] or the breast alone may be missing, with a rudimentary nipple, which is usually displaced either upward or downward and inward (Fig. 1). The pectoralis major is at times replaced by a fibrous band over which the skin becomes rolled, giving rise to a sickle-shaped fold which forms the anterior axillary wall. Roentgenograms of the chest are negative.[12] Accompanying skeletoanomalies are not infrequent, especially hypoplasia of the shoulder girdle and arm, Sprengel's deformity, hypophalangia, and syndactilism. There may also be a marked asymmetry of the chest in some cases, due to defects in the cartilaginous portion of the second and third ribs on the affected side.

Compensatory action in other muscles usually serves to preclude any disability resulting from pectoral deficiencies, and there are reported cases of a pitcher and of a fencer, each of whom preferred the

use of his defective arm.[11] Occasional instances are encountered where function of the arm and shoulder are considerably impaired (Case 1).

Since the pectoralis major is of value in forced inspiration, it would seem likely that an absence or depletion of muscle substance might well produce some limitation in chest expansion, thus diminishing vital capacity of the individual. Such a condition was found to obtain in both of the cases included in this communication; in Case 1, with disability present, chest mobility was notably slight. Such a finding is of little significance during health, but in the event of a disease process accompanied by excessive dyspnea any decrease in the functional capacity of the accessory respiratory muscles becomes a factor worthy of consideration.

In regard to the origin of pectoral agenesis, heredity does not appear pertinent. Only once has the abnormality been noted in more than one member of a family—a case of father and two sons[13]—although other developmental defects, particularly syndactilism, are quite often seen in the same family. The most widely accepted view concerning the embryologic cause of the condition is that advocated by Lewis,[14] who believes it is due either to a failure of attachment and subsequent atrophy of the pectoralis minor and sternocostal portion of the pectoralis major, or to a lack of complete differentiation between the two muscles. Jones[11] feels that, while both factors may be contributory, in favor of the latter view is the fact that when the clavicular head of the pectoralis major remains, there is always marked hypertrophy of this portion.

Treatment is not required unless disability is present or chest expansion shows considerable impairment. In cases of this type corrective exercises designed for the purpose of stimulating compensatory muscular hypertrophy should be introduced. The patient in Case 1 illustrates that beneficial results are obtainable from such a regimen, providing cooperation is maintained throughout.

CASE 1.—W. G., a boy twelve years old, born of American parentage, was first seen in June, 1934, because of an inability to defend himself in physical combat with children much smaller than himself. There was no history of chronic familial or hereditary disease, and maternal health throughout pregnancy had been good. An older brother was living and well, and no other members of the family had any developmental defects. The patient was delivered at term following an easy labor, and the birth weight was 8 pounds 9 ounces. His postnatal course was uneventful, but it was noted during the first weeks of life in bathing him that the left half of the chest appeared flat. In the ensuing years growth and development were normal, and general health had been exceptional. For some time, however, it had been apparent that he was unable to perform physical feats that other boys of his age could accomplish with ease and dispatch. Although not unwilling to fight, he always came out a poor loser on such occasions. The child had never been able to swim more than a few strokes owing to difficulty in satisfactory manipulation of his left arm.

Examination showed a very well-nourished and well-developed boy of twelve years who looked healthy. General muscle tone was satisfactory, and the only abnormal findings related to the thorax. Inspection of the chest showed a marked asymmetry with infraclavicular flatness on the left. There was an atrophic appearance to the left pectoral muscles. The nipple on that side was rudimentary and displaced toward the midline and upward. Palpation disclosed a complete absence of the three lower portions of the pectoralis major muscle and an absence of the pectoralis minor. The remaining clavicular head of the muscle was moderately hypertrophied. There was no hypertrophy of the deltoid. Extension of the arms produced a hori-

Fig. 1.—W. G., absence of sternal, costal, and abdominal portions of left pectoralis major muscle. Note thoracic asymmetry and rudimentary appearance of left nipple, which is displaced upward and inward.

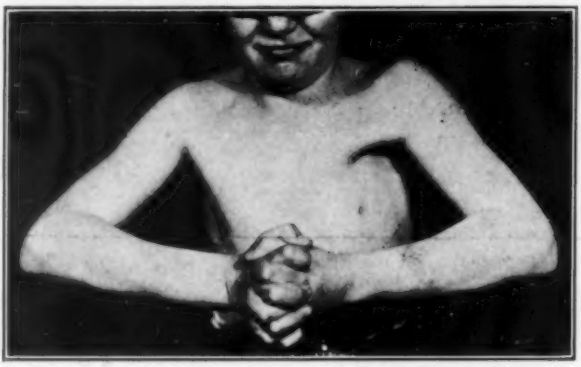

Fig. 2.—W. G., observe horizontal anterior axillary fold and compensatory hypertrophy of remaining clavicular portion of left pectoralis major muscle.

zontal anterior axillary fold (Fig. 2). Chest girth taken at the nipple line midway between expiration and inspiration was 27 inches, contracted 26 inches, expanded 27.75 inches. Muscular power in the left arm was definitely diminished.

The child was placed upon a systematic schedule of corrective exercises and seen at periodic intervals throughout the following year. Mental and physical improvement were apparent within a few weeks. When he was last examined in May, 1935, the deltoid on the left had undergone moderate hypertrophy as well as the clavicular portion of the left pectoralis major and the right pectoral muscles. Chest girth midway between inspiration and expiration was 27.25 inches—contracted 26.25 inches

—expanded 28.50 inches. The left arm was still weak but showed improvement. The child stated that his arm felt much stronger and that he was now able to perform on a horizontal bar and do other things that had previously been accomplished with difficulty.

CASE 2.—E. K., a ten-year-old-boy of Irish-American parentage, was seen in March, 1935, because of moderate malnutrition and poor appetite. There was no known history of chronic familial or hereditary disease. Both parents were well, and a brother, two years younger, was in good health. No members of the family had any evidence of developmental defects. His past history was not remarkable. Although he was never especially robust, his growth and development had been essentially normal. His appetite was inclined to be fickle, and his mother felt that he had always been somewhat underweight. During the course of examination his

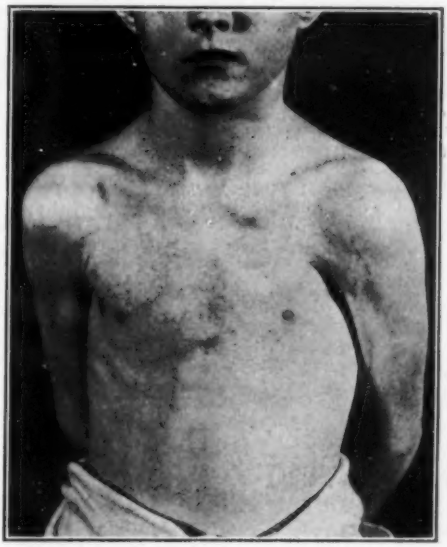

Fig. 3.—E. K., partial absence of left pectoral group. The left anterior axillary fold is formed by hypertrophic fibers of the deltoid and clavicular head of the pectoralis major muscles.

thoracic asymmetry called attention to a left pectoral defect. There was an absence of the lower two-thirds of the left pectoralis major and a complete absence of the pectoralis minor. The right pectoral group was intact. The remaining clavicular portion of the left pectoralis major was moderately hypertrophic, and the deltoid on the same side had also undergone compensatory hypertrophy, the left anterior axillary fold being formed by these two muscles (Fig. 3). The child had never suffered any disability from his abnormality, and there was no demonstrable weakness of the left arm. Chest expansion was 1.75 inches.

SUMMARY

Congenital muscular defects are not extremely rare, and a variety of these abnormalities have been reported, of which abdominal amyogenesis and congenital absence of the pectoral muscles are of greatest

clinical interest. The former is often incompatible with life when the deficiency is extensive; in the latter, considerable disability may obtain unless compensatory hypertrophy has occurred.

A review of the literature pertinent to these conditions is presented, and two additional cases of partial absence of the left pectoral muscles are contributed.

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CARCINOMA OF THE THYROID GLAND IN CHILDREN

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INCIDENCE

CARCINOMA of the thyroid gland among children, aged fourteen years and younger, is of rare occurrence. No exact knowledge of its frequency is obtainable. An idea of the relative frequency among young individuals as compared to that among individuals of all ages is obtained from the figures of Pemberton, who reported 276 cases in which carcinoma of the thyroid gland was treated operatively at the Mayo Clinic. In one of these cases the patient was in the first decade of life, and in two of the cases the patients were in the second decade of life. Thus it may be said that approximately 1 per cent of carcinomas of the thyroid gland affect children. This does not take into account the possibility that, in some cases in which carcinoma of the thyroid gland has been found to affect older individuals, the lesion may have appeared first in childhood; neither does it signify that preexisting lesions, such as adenomas, may have been present from an early age in some cases.

An attempt was made at the clinic to determine the relative incidence of carcinoma of the thyroid gland and exophthalmic goiter among children aged fourteen years or less. Eight instances of carcinoma of the thyroid gland and 157 instances of exophthalmic goiter were noted among these children in the same period. In other words, carcinoma of the thyroid gland was slightly more than a twentieth as frequent among these children as was exophthalmic goiter. Although it may be largely a coincidence, it was of extreme interest to find that the ratio of the incidence of both carcinoma of the thyroid and of exophthalmic goiter among children and among adults was approximately 1 to 100.

A summary of the American literature for twenty years reveals reports of six cases in which carcinoma of the thyroid gland affected children. Three of these were reported by Cattell; one was reported by Hughes, one by Schultz, and one by Lee. Demme, from Bern, said that carcinoma of the thyroid gland is an extremely rare lesion among children. Although he had seen two instances of sarcoma of the thyroid gland, he had not had any experience with carcinoma of the thyroid among children.

Sex incidence.—Pemberton found malignant disease of the thyroid gland to be twice as frequent among females as it was among males,

From the Section on Pediatrics, the Mayo Clinic.

and in the present series of eight cases, seven of the patients were girls and one patient was a boy. Obviously, the group is much too small to be used as an absolute basis for comparison, but it at least indicates that the incidence of carcinoma of the thyroid gland is higher among female children than it is among females of other ages.

REPORT OF CASES

CASE 1.—A girl, aged twelve years, came to the clinic on Aug. 10, 1909, because of a tumor in the neck (Fig. 1). The tumor had been noticed first when the patient was two years of age. It had caused dyspnea on exertion. When the girl was nine years old, a portion of the mass in the right lobe of the thyroid gland had been removed, but the growth of the tumor had continued. The only symptoms at the

Fig. 1. Fig. 2.

Fig. 1.—Carcinoma of thyroid gland. Scar of previous operation is visible.

Fig. 2.—Photomicrograph showing papillary adenocarcinoma, grade 1, of thyroid gland of patient in Case 1 (×135). Formation of acini is shown clearly.

time the patient was seen first at the clinic were local discomfort, which was caused by the tumor, and some hoarseness. Operation, which was performed in August, 1909, revealed a large colloid cystic goiter. Multiple cysts were found in both lobes and in the isthmus. There was carcinoma in one portion of the tumor. Thyroidectomy with enucleation of multiple cysts was carried out. The pathologic diagnosis was papillary adenocarcinoma, grade 1 (Fig. 2).

On April 21, 1913, the patient returned to the clinic. She said that she had felt well and that she had attended school regularly. In the year previous to this the goiter had reappeared and had increased slowly in size. The right lobe measured 2 by 2.25 cm., the middle lobe measured 1 by 1.5 cm., and the left lobe measured 1.5 by 2.5 cm. Palpation did not reveal any very hard or infiltrating masses, which might suggest the presence of carcinoma. There was no paralysis of the vocal cords.

Operation was carried out on April 23, 1913. Three masses, each the size of a lemon, were removed from the right side of the neck, and one mass, the size of a

walnut, was removed from the left side of the neck. The pathologic diagnosis was papillary adenocarcinoma, grade 1.

In October, 1919, the patient again returned to the clinic. She had married in the interval since her visit to the clinic in 1913, had been pregnant, and had been delivered without incident. The thyroid enlargement had recurred. Her hoarseness was of about the same degree as it had been at the time of her last visit to the clinic, but there was not any dyspnea. There was a moderate degree of anemia. The basal metabolic rate was +10 per cent. A diagnosis of multiple recurring adenomas of the thyroid gland with fair possibility of malignant degeneration was made. Operation was performed on Oct. 16, 1919. The right lobe of the thyroid gland was found to be about six times the normal size. It was practically impossible to save any glandular tissue on the right side. On the left side, glandular tissue, which corresponded in size to that of a normal lobe, was preserved. The operation was difficult because of adhesions from previous operations. The pathologic report was papillary adenocarcinoma, grade 1.

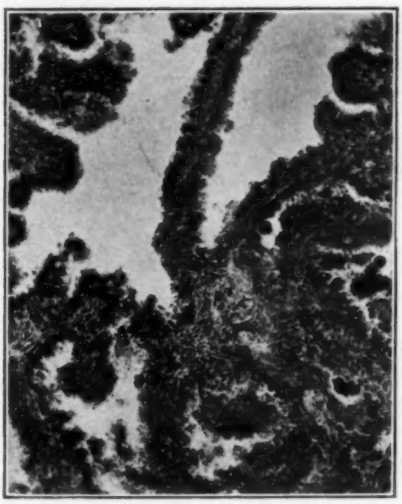

Fig. 3.—Photomicrograph of adenocarcinoma, grade 2, of right lobe of thyroid gland of patient in Case 2 (×135).

In 1927, she was doing well; however, in that same year, notice was received of her death, but the cause was not stated.

CASE 2.—A girl, aged eight years, was brought to the clinic on July 15, 1924, because of enlarged lymph nodes in the right side of the neck. Her family history was unimportant. She had had her tonsils and adenoids removed in 1921 and had undergone an appendectomy in 1922. In July, 1921, from three to four months after her tonsillectomy, a swelling had been discovered in the right side of her neck. Three or four weeks later, a physician had made a diagnosis of "enlarged glands." These had increased in size, and other lymph nodes in the right side of the neck had become enlarged.

Examination revealed a rather large lymph node and several smaller ones, which were elastic, discrete, and gave rise to a suspicion of Hodgkin's disease. The left epitrochlear and right axillary lymph nodes were palpable. Urinalysis and examination of the blood did not reveal anything abnormal. The tuberculin test was

negative. A definite clinical diagnosis was not made. On July 18, 1922, a lymph node was removed for diagnosis. This revealed a papillary carcinoma, and the pathologist recommended examining the kidneys, ovaries, thyroid gland, and nasopharynx, for the primary carcinoma.

On Jan. 1, 1927, the patient returned to the clinic. At this time there was a small swelling on the right side of the neck, which had been noticed a short time after her operation in July, 1922, and which had been gradually growing larger. There was found just above the clavicle an enlarged lymph node, which moved up and down when the patient swallowed. Urinalysis, examination of the blood, and roentgenologic examination of the thorax did not reveal any abnormality.

A subtotal thyroidectomy was performed on Jan. 12, 1927. The right lobe of the thyroid gland was enlarged to about three times the size of a normal lobe, and a definitely circumscribed portion of this lobe revealed malignancy (Fig. 3). One lymph node in the median line of the neck, and several in the jugular region were found to be affected by carcinoma and were removed. The posterior part of the right lobe of the gland, which was about a fifth of the size of a normal lobe, was preserved. The left lobe was apparently normal. The pathologic report was carcinoma of the thyroid gland with metastatic involvement of the cervical lymph nodes.

Radium was placed in the drainage tube after the operation. This was supplemented with the external application of radium packs. Radium therapy was repeated in April, 1927; in June, 1927; and in August, 1927.

In August, 1933, six and one half years after operation, the patient returned to the clinic. Six months previously a carious lower right molar tooth had been extracted, and one month previously two lower left molar teeth had been extracted. Since that time there had been a palpable lymph node in the left submental region, and the patient said that there had been a similar lymph node in the right submental region since 1927. A sequestrum was found at the site of extraction of the two left lower molar teeth. No other involvement of lymph nodes and no evidence of recurrence of the thyroid carcinoma could be found. Roentgenologic examination of the thorax did not reveal any metastatic involvement.

CASE 3.—A girl, aged nine years, was brought to the clinic on June 29, 1926, because of goiter. The family history was irrelevant. The patient had had diphtheria, influenza, and tonsillitis. In 1923 her tonsils and adenoids had been removed, and in 1920 her appendix had been removed. Since the appendectomy, in December, 1920, she had suffered from hoarseness, which had increased in severity so that when she cried she often choked and became dyspneic. In April, 1926, thyroid trouble had been diagnosed, and she had been given medicine until two weeks before she came to the clinic. Her neck was known definitely to have been enlarged since April, 1926. Three efforts had been made to operate on her, but each time she had offered so much resistance when she had been placed on the operating table that the operation had not been performed.

Examination showed her to be well developed and well nourished. There were three enlarged lymph nodes on the right side of the neck and two on the left side. They were not tender and were not fixed. The left vocal cord was found to be fixed in the median line, and hoarseness was evident when she spoke. Urinalysis and examination of the blood did not reveal any abnormality. The Wassermann reaction of the blood and the tuberculin test were negative. A roentgenogram of the thorax did not reveal anything abnormal. Her basal metabolic rate was −20 per cent. The condition was thought to be either a lymphosarcoma or Hodgkin's disease. A clinical diagnosis of bilateral cervical adenopathy with obstructive dyspnea and hoarseness was made.

Operation was performed on July 5, 1926. Examination by the surgeon revealed a diffuse, hard enlargement of the neck in the region of the thyroid gland; this was thought unquestionably to be malignant. A specimen was removed for diagnosis. The pathologic diagnosis was adenocarcinoma, grade 2, of the thyroid gland (Fig. 4).

Radium therapy was administered. Convalescence was uneventful. The voice improved within four weeks, and the breathing became less dyspneic. She resumed her school work.

She returned to the clinic on Sept. 14, 1926. Her general health was excellent. There had been slightly greater dyspnea during the three weeks preceding this visit than there had been immediately before this. Examination revealed hard, firm, nodular masses in the anterior portion of the neck. The breath sounds were rather harsh. A roentgenogram of the thorax did not reveal anything abnormal. Radium therapy was repeated.

Fig. 4.—Photomicrograph of papillary adenocarcinoma, grade 2, of thyroid gland of patient in Case 3 (×175).

Her general condition remained good. Radium therapy was administered at intervals until August, 1928. Her weight increased progressively. In July, 1927, one year after operation, she was 10 pounds (4.5 kg.) overweight. In November, 1927, a roentgenogram of the thorax showed questionable metastatic involvement of the lungs. By February, 1928, she was 25 pounds (11.3 kg.) overweight. There were some small masses on either side of the neck. In May, 1928, the multiple metastatic growths in the thorax were more pronounced than they had been in the previous November. In December, 1928, her general health appeared good, and she had continued to attend school regularly. In February, 1930, she returned, and said that she felt well but that she had been bothered by her excess weight. Although her appetite had not been excessive she had gained 12 to 14 pounds (5.4 to 6.4 kg.) during the month preceding this visit. Her weight was 144 pounds (65.3 kg.), and her height was 51 inches (129.5 cm.). Her basal metabolic rate was −47 per cent. She exhibited features of frank myxedema. Administration

of desiccated thyroid in doses as large as 4 grains (0.24 gm.) daily controlled the myxedema and raised the basal metabolic rate nearly to the average value.

In August, 1934, she was found to have some increase in difficulty in swallowing solid foods. The local condition in the neck had not changed materially. A cough which was more marked at night than it was during the day had developed. This sometimes occurred in paroxysms, which lasted up to two hours. She began to raise a white purulent sputum, but no blood. Fatigue, exhaustion, and shortness of breath were present. Her weight was 133 pounds (60.3 kg.). The cervical lymph nodes on either side were small and calcified. Examination of the lungs did not disclose any râles or areas of dullness, but there was increased vocal and tactile fremitus, and considerable bronchial breathing in both lungs. Roentgenograms showed an increase in the size and density of the multiple metastatic growths in the lungs (Fig. 5).

CASE 4.—A girl, aged seven years, was brought to the clinic on July 28, 1926, because of a swelling in the neck, which had been present for a year. The parents

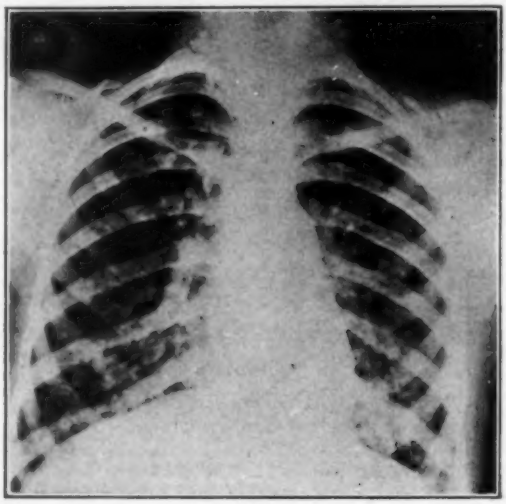

Fig. 5.—Roentgenogram of thorax of patient in Case 3; this was made thirteen and a half years after the onset of carcinoma of thyroid gland and shows metastatic involvement of both lungs and calcification of tissues in the neck.

were living and well. The paternal grandfather had died of cancer. The patient had had tonsillitis in 1925 and whooping cough in 1926. In April, 1925, a small swelling had been noted in the region of the isthmus of the thyroid gland. This gradually had increased in size until the time the patient came to the clinic. While the patient had suffered from pertussis, in the year previous to her registration at the clinic, the mass had seemed to increase in size rather rapidly. There had not been any pain, dyspnea, or dysphagia.

Examination showed her height to be 44 inches (111.7 cm.) and her weight 44 pounds (20 kg.). The average weight for her height and age, according to the Wood-Baldwin tables, is 42 pounds (19.1 kg.). The pulse rate was 90 beats per minute. The Wassermann reaction of the blood and the tuberculin test were negative. In the thyroid gland was a mass which occupied a portion of the right lobe and the right side of the thyroid isthmus (Fig. 6). The mass was about

3 cm. in diameter and firm, and it moved with deglutition; it was not tender. The lesion was thought to be an adenomatous goiter.

On Aug. 7, 1926, operation was performed. The right lobe of the gland contained an encapsulated tumor about 6 or 7 cm. in diameter, which was thought to be an adenoma. The right lobe was resected, but a portion of the posterior part, which amounted to about a fourth of a normal sized lobe, was preserved. The left lobe was normal in size and was not disturbed.

The pathologic diagnosis was, adenocarcinoma, grade 1, in a fetal adenoma (Fig. 7). The tumor measured 2 by 3 by 5 cm.

Radium was applied and the wound healed promptly. On Oct. 3, 1934, a report was received that the child was well.

CASE 5.—A boy, aged fourteen years, was brought to the clinic on Oct. 29, 1930, because of failure to grow and because of a small mass in the neck. His family history was unimportant. His birth had been normal. He had not been

Fig. 6.

Fig. 7.

Fig. 6.—Mass in region of isthmus of thyroid gland of patient in Case 4; duration, one year.

Fig. 7.—Photomicrograph of section of mass in Fig. 6, showing adenocarcinoma, grade 1, in fetal adenoma, with slight papillary formation (×155.)

breast fed. He had been nourished with malted milk and later with a barley food. He had been fat and overweight when he was an infant. The deciduous teeth had appeared at the usual time, but they had decayed rapidly. From eighteen months of age until three years of age, he had been very obese. He had not walked until he was four and a half years of age. He was said to have had rickets. A thyroid preparation had been administered for eight months. During the time that the thyroid substance had been administered, he had spells of unconsciousness, which had lasted about ten to fifteen minutes and had occurred about once a day. After the administration of the thyroid preparation had been discontinued, the unconscious spells had recurred only once. After he was three years old, he had lost weight rapidly and had become very thin. For the two years previous to his admission to the clinic, he had failed to grow or to gain in weight.

Two years previous to his admission to the clinic, his tonsils and adenoids had been removed, and at that time a small lump had been noted in his neck. This mass had increased in size up to the time of his admission to the clinic. In July, 1930, three months before his admission to the clinic, thyroid tablets had been administered twice a week, and two drops of solution of iodine had been administered once a week. This medication had been continued for four weeks. During the month before his registration at the clinic, he seemed much better than he had been before, and he had gained from 4 to 5 pounds (1.8 to 2.3 kg.). He had been attending school and had been receiving fairly good grades.

Examination showed him to be a slender undernourished boy. His height was 56 inches (142.2 cm.) and his weight was 57 pounds (25.9 kg.). The average weight for his height and age, according to the Wood-Baldwin tables, is 74 pounds (33.6 kg.). The systolic blood pressure was 98 and the diastolic pressure, 60.

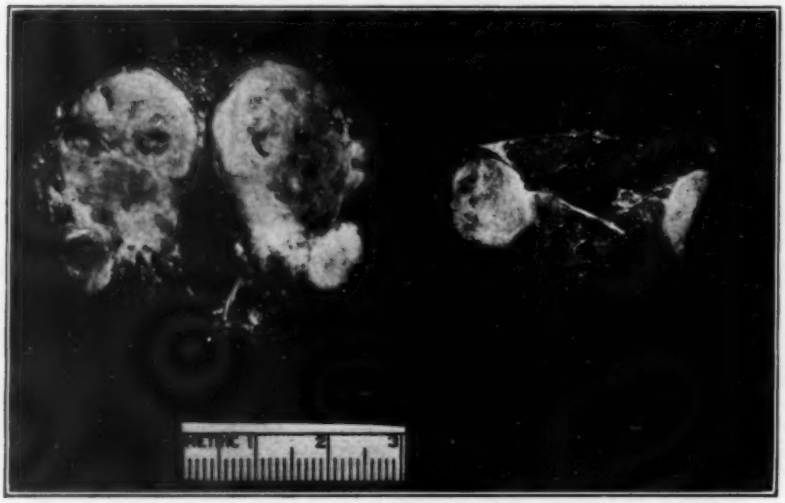

Fig. 8.—Masses removed from right and left lobes of thyroid gland of patient in Case 5.

His pulse rate was 78 beats per minute. His temperature taken orally was 98° F. There was a developmental malformation of the teeth. Scoliosis with deformity of the thorax was evident. The feet were poorly shaped and pronated. In the upper part of the right lobe of the thyroid gland there was an irregular firm nodule which measured about 2.5 cm. in diameter; in the isthmus there was a very small nodule; and in the left lobe there was a nodule about the size of a pea. The urine and the blood were normal. The tuberculin test and the flocculation test for syphilis were negative. The basal metabolic rate was −6 per cent. Roentgenograms of the head and thorax did not reveal anything abnormal. Roentgenograms of the spinal column showed a scoliosis in the thoracolumbar region. A roentgenogram of the neck showed a tumor of the soft tissue in the region of the thyroid. This tumor contained a calcified area and was thought to be a calcified granuloma. On palpation, the mass did not feel like an adenoma, and it appeared most likely that it was a tuberculous lesion. However, there was no good basis for expressing any opinion.

On Nov. 6, 1930, the thyroid gland was subjected to surgical exploration. A tumor about the size of a lime was found in the upper pole of the right lobe of the gland. The portion of the right lobe which contained the tumor was resected. The tissue which was removed from the right side measured 2.5 by 2.5 by 4 cm. (Fig. 8). The thyroid tissue, which was about a fifth or a sixth the size of a normal lobe, was preserved. There also was a small tumor in the upper pole of the left lobe. The portion of the left lobe which contained the tumor was resected. The resection was carried well into healthy tissue on all sides of the tumor. The thyroid tissue which was removed from the left side measured 1 by 2 by 2.5 cm. (Fig. 8). The combined weight of the thyroid tissue which was removed from both sides was 24 gm. The pathologic report was multicentric adenocarcinoma, grade 2, involving both lobes of the thyroid gland (Fig. 9). The larger carcinoma was on the right side.

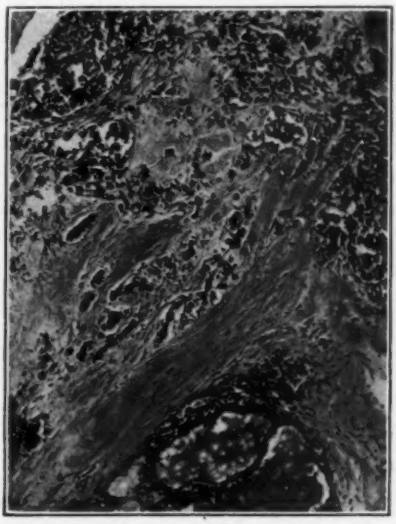

Fig. 9.—Photomicrograph of multicentric adenocarcinoma, grade 2, of thyroid gland of patient in Case 5.

His condition at present is good. A few shotty lymph nodes are palpable in the neck, but there is not any evidence of recurrence of the carcinoma.

Case 6.—A girl, aged thirteen years, came to the clinic in October, 1932, because of tumors of the thyroid gland, which had been present for six years. The family history was not significant. In 1927 the patient had had measles; otherwise, the past history did not reveal anything important. In 1926, six years before her registration at the clinic, her parents first had noticed an irregular enlargement of the thyroid gland, which had increased slowly. It had moved with the act of swallowing. There had not been any pain or hoarseness but sometimes the patient had experienced a feeling of pressure in the neck. In September, 1931, she first had noticed that she became fatigued easily, especially when she walked upstairs. There had not been any anorexia, cough, loss of weight, palpitation, tremor, or rapid increase in the size of the tumor. In October, 1932, the tumor had attained the size of an orange (8 cm. in diameter), and operation had been performed elsewhere. A small piece of tissue had been removed for biopsy. The

tumor had been found to have invaded the vocal cords, and its removal had not been attempted. On October 18, 1932, she had received one roentgenologic treatment.

Examination at the time of her registration at the clinic revealed that her height was 5 feet (152.4 cm.) and that her weight was 103 pounds (46.7 kg.). The normal weight for her height and age, according to the Wood-Baldwin tables, is 115 pounds. The systolic blood pressure was 110 and the diastolic blood pressure, 60. Her pulse rate was 100 beats per minute. Her temperature, taken by mouth, was 99.6° F. A large, firm tumor involved the thyroid gland; this was more prominent on the left than on the right (Fig. 10). The tumor moved slightly during the act of deglutition. There was bilateral enlargement of the cervical lymph nodes. Pathologic report (from examination of the tissue removed elsewhere in October, 1932) was papillary adenocarcinoma, grade 1 (Fig. 11).

Fig. 10. Fig. 11.

Fig. 10.—Carcinoma of thyroid gland; appearance of patient in Case 6, eight years after onset of disease. Opening of cystic mass can be seen in upper margin of projecting tumor; scar of previous operation also can be seen.

Fig. 11.—Photomicrograph of papillary adenocarcinoma, grade 1, of thyroid gland of patient in Case 6 (×135).

Roentgenotherapy was administered in October, 1932, May, 1934, and September, 1934. For about a year following the first course of roentgenotherapy, the size of the tumor was practically unchanged. In December, 1933, a sinus formed spontaneously in the upper part of the mass, from which a watery yellow material drained for about a day. In April, 1934, she experienced two periods of weakness, nausea, sweating, and chilliness, which began in the evening and lasted several hours. There was not any pain.

In May, 1934, examination revealed a cystic tumor the size of a large walnut. This was situated in the median line of the neck, over the thyroid isthmus. A healed sinus was seen just below the hyoid bone. The left lobe of the thyroid gland was extremely hard and fixed. The cyst was aspirated and approximately 20 c.c. of clear, amber fluid was withdrawn. Roentgenotherapy was administered.

In September, 1934, the patient returned to the clinic. She had felt well until

about three weeks before this admission, when she had experienced nervousness, tachycardia, headache, and anorexia, and had lost 12 pounds in weight. She had remained in bed for about ten days. Although her condition had improved, she had not regained any of the lost weight. The size of the tumor was about the same as it was at the time of her previous visit to the clinic in May, 1934. Roentgenograms of the lungs did not show any evidence of metastatic lesions. The urine and blood were normal. The tuberculin test and the Wassermann reaction of the blood were negative.

CASE 7.—A girl, aged eight years, complained of enlarged cervical lymph nodes, which had been present for four months. The family history was unimportant. She had had scarlet fever in 1930 and pneumonia in 1932. Her tonsils and adenoids had been removed in 1930. For a year previous to her admission to the clinic, she had not been feeling as well as usual. During the four months previous to

Fig. 12. Fig. 13.

Fig. 12.—Appearance of mass in left side of neck of patient in Case 7, four months after it had been discovered. Scar of operation for removal of lymph node for biopsy is visible.

Fig. 13.—Photomicrograph of papillary adenocarcinoma, grade 2, of lymph node, which was removed from patient in Case 7 (×215).

her admission to the clinic, there had been a gradual increase in the size of the lymph nodes on both sides of the neck. There had not been any dysphagia, but there had been slight hoarseness at times. However, when the hoarseness had been present there also had been evidence of a slight infection of the upper part of the respiratory tract.

Examination revealed that she was 51.75 inches (131.3 cm.) in height and weighed 51 pounds (23.1 kg.). The normal weight for a girl of her height and age, according to the Wood-Baldwin tables, is 64 pounds (29 kg.). The systolic blood pressure was 82 and the diastolic blood pressure, 44. Her temperature was 99.6° F., taken by mouth. Her pulse rate was 88 beats per minute. The lymph nodes on both sides of the neck were moderately enlarged, firm, and discrete, but were not tender. Those on the right side were larger than those on the left (Fig.

12). There was a slight, moderate, symmetrical enlargement of the thyroid gland.

On Aug. 30, 1934, a lymph node from the left posterior triangle of the neck was excised. Pathologic examination of the lymph node showed a carcinoma, grade 2 (Fig. 13), which was thought to be secondary to a carcinoma of the thyroid gland.

Roentgenotherapy was administered in September, 1934. This was followed by a marked decrease in the size of the lymph nodes and of the thyroid gland. The roentgenotherapy was repeated in December, 1934. The condition of the patient at present is good; the disease has been present now for nine months.

CASE 8.—A girl, aged seven years, was brought to the clinic on Oct. 27, 1934, because of a swelling in the neck which had been present for two and a half years. One grandmother has goiter. There was no knowledge of any carcinoma in the family. At six years of age her tonsils and adenoids had been removed. At seven years of age she had had whooping cough, bronchitis, and pneumonia. In July,

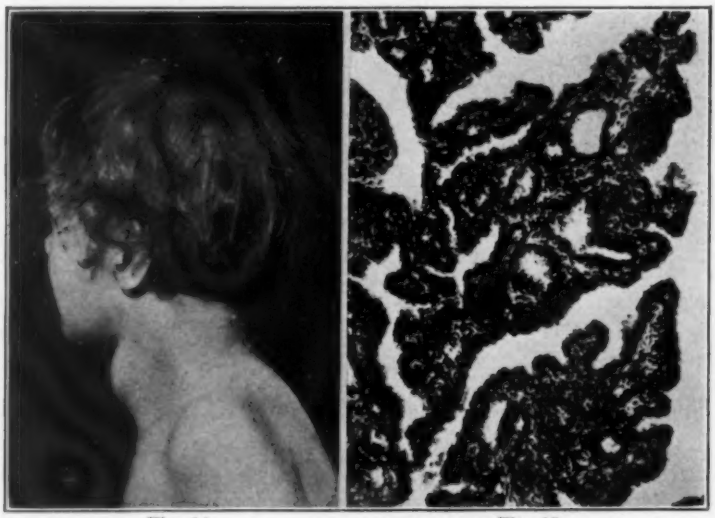

Fig. 14. Fig. 15.

Fig. 14.—Appearance of patient in Case 8, two years after mass in left side of neck was first noticed.

Fig. 15.—Photomicrograph of papillary adenocarcinoma, grade 1, in fetal adenoma in neck of patient in Case 8 (×130).

1932, a small lump had been noticed in the neck, just to the left of the median line. The lump had been present constantly thereafter; it had appeared somewhat larger at some times and slightly smaller at other times. For the six months preceding her registration at the clinic, it had remained about the same size. There had not been any pain or tenderness. The skin overlying the mass had been normal. There had not been any dyspnea or dysphagia. About eight months before registration, the mass had appeared to grow rapidly during an attack of pneumonia. She had not received any treatment for this mass.

Examination revealed a girl who was 50 inches (127 cm.) in height and who weighed 54.5 pounds (24.7 kg.). The average weight for a child of her age and height, according to the Wood-Baldwin tables, is 56 pounds (25.4 kg.). The systolic pressure was 105, and the diastolic pressure was 70. The pulse rate was 90 beats per minute, and the temperature was 98° F. by mouth. She was well de-

veloped and well nourished. There was not any exophthalmos. To the left of the median line of the neck, there was a visible and palpable mass, which measured 3 by 5 cm. (Fig. 14). The mass felt soft, but it was not definitely cystic. It was not tender and was not adherent to the skin. The left margin of the mass seemed to extend below the left sternocleidomastoid muscle. The blood and urine were normal. The tuberculin test and the Wassermann reaction of the blood were normal. Roentgenologic examination of the thorax did not reveal any abnormality. It was believed that the lesion possibly was a cyst of the thyroglossal duct.

Operation, which was performed on October 30, 1934, revealed a tumor in the left lobe of the thyroid gland, near the superior pole. The tumor was oblong in shape and measured about 3 by 3 by 6 cm. The left lobe of the thyroid gland was resected, and only tags of thyroid tissue were left. It was the opinion of the surgeons at the time of operation, that the tumor was unquestionably a papillary adenocarcinoma. The tissue which was removed measured 3 by 4.5 by 7.5 cm., and weighed 34 gm. A pathologic diagnosis of papillary adenocarcinoma, grade 1, in a colloid and fetal adenoma was made (Fig. 15). Radium therapy was administered by means of surface packs, and the child was permitted to return home.

ETIOLOGY

The etiology of carcinoma of the thyroid gland is unknown. In nearly all descriptions of the condition, however, it has been pointed out that in a very large percentage of cases the carcinoma occurred in a preexisting lesion, which usually was an adenoma. Pemberton found that in 87 per cent of cases of malignant neoplasms, the tumor originated in preexisting goiter. Adenomas of the thyroid gland are not rare among the population as a whole. Inasmuch as visible or palpable adenomas do not occur with nearly so great frequency among children as among older individuals, they may play a lesser rôle as precursors of carcinoma among young patients.

In this series of eight cases, the occurrence of preexisting adenoma was not frequent. In Cases 4 and 8 the carcinomas were found in fetal adenomas. In Cases 2 and 7 there was not any nodular enlargement of the thyroid gland when the patients registered at the clinic. This excludes the possibility of a preexisting lesion of clinically demonstrable extent. In the Cases 1, 3, 5, and 6 the histories, the findings at operation, and the pathologic appearance of the tissues indicated that the carcinomas did not have their origin in adenomas.

Trauma is the other factor to which attention has been directed as a cause of carcinoma of the thyroid gland. It is true in many instances that the patient or the patient's parents can recall that a blow, or some other form of direct trauma to the neck, was sustained at some time previous to the discovery of an enlargement of the thyroid gland or the regional lymph nodes. That such trauma played any part in the etiology of a neoplastic process must obviously be considered an open question.

TABLE I

FEATURES OF CARCINOMA OF THYROID GLAND AMONG CHILDREN

CASE	SEX	AGE IN YEARS	AGE IN YEARS AT ONSET	TUMOR OF THYROID	ENLARGED CERVICAL LYMPH NODES	HOARSENESS OR DYSPNEA	INVOLVEMENT OF CERVICAL LYMPH NODES	DISTANT METASTASIS	GRADE OF MALIGNANCY	LOCAL RECURRENCE	EVIDENCE OF INVASION	DURATION OF DISEASE FROM FIRST SYMPTOM, YR.	DURATION OF LIFE AFTER FIRST TREATMENT, YR.	PRESENT CONDITION OF PATIENT	TYPE OF CARCINOMA
1	F	12	2	+	0	0	0	0	1	+	0	28	24	Dead	Papillary adenocarcinoma
2	F	8	5	0	+	0	+	0	2	0	0	14	10	Living, well	Adenocarcinoma
3	F	9	3	+	0	+	0	+	2	+	+	15	9	Living, fairly well	Papillary adenocarcinoma
4	F	7	6	+	0	0	0	0	1	0	0	9	8	Living, well	Adenocarcinoma in fetal adenoma, with slight papillary formation
5	M	14	12	+	0	0	0	0	2	0	0	7	5	Living, well	Multicentric adenocarcinoma
6	F	13	7	+	0	0	0	0	1	+	+	8	2	Living, fairly well	Papillary adenocarcinoma
7	F	8	8	0	+	0	+	0	2	0	0	9 mo.	5 mo.	Living, well	Papillary adenocarcinoma
8	F	7	4½	+	0	0	0	0	1	0	0	3	3 mo.	Living, well	Papillary adenocarcinoma in fetal adenoma

SYMPTOMS AND SIGNS

The symptoms and signs of carcinoma of the thyroid gland among children naturally depend largely on the extent of the lesion. Early evidence consists almost entirely of enlargement of a part of the thyroid gland, or of enlargement of adjacent lymph nodes. The enlargement of the gland itself is irregular and the appearance of a mass in one part of the gland may be the only indication of a possible malignant lesion. It is possible, as in two of the cases reported here, that enlargement of the cervical lymph nodes, which may become involved metastatically, may be evident for a considerable time before any involvement of the thyroid gland itself can be determined.

The characteristics of the mass or masses, which constitute malignant foci, vary with the type of carcinoma. The prominence and apparent consistence will depend on the situation of the tumor in the thyroid gland; that is, on the amount of overlying normal tissue. Obviously, the characteristics will be more readily determinable, the closer the tumor is to the surface. Although usually firm, hard, and irregular, the tumor may be quite smooth, rather soft, and, as in one instance reported here, may exhibit a cystic quality.

The finding of a mass in the thyroid gland, regardless of its characteristics, is insufficient to warrant a diagnosis of malignancy. However, among children, benign tumors of the thyroid gland have been found less frequently than have malignant tumors, and hence any mass, however innocent appearing clinically, should be suspected of having malignant qualities.

Symptoms and signs, which are ordinarily considered as indicative of malignant disease of the thyroid gland, do not appear until there has been extension of the growth and involvement of surrounding tissues. There results an irregular, usually firm, tumor or tumors, which are unilateral or bilateral, are fixed, and may or may not be accompanied by enlargement of cervical lymph nodes. Hoarseness, dyspnea, and a sense of pressure in the neck may be present. Systemic effects of the disease usually are not evident until extensive local involvement or metastatic involvement has taken place. That the neoplastic tissue possesses any function characteristic of the thyroid gland is a controversial subject. The characteristic features are given in Table I.

Sudden rapid growth of a preexisting mass is said to be a strong indication of the malignant nature of such lesions. It probably is a significant sign if the patient is an adult, but, in these cases in which the condition affected children, it was not noted as a frequent occurrence.

METASTASIS

There is some difference of opinion as to the sites of predilection for metastatic involvement which follows carcinoma of the thyroid gland. In 438 cases, Pemberton found that the regional lymph nodes were involved in 69.5 per cent, the lungs in 24 per cent, the thorax and mediastinum in 16 per cent, and the bones in 5 per cent. Other less frequently affected parts of the body were the axilla, the liver, the trachea, the brain, the esophagus, the kidneys, and the scalp. He pointed out that in the presence of malignant disease, including carcinoma and sarcoma, of the thyroid gland, metastatic involvement takes place by way of the blood and lymph streams and that there may be single or multiple primary lesions.

In the eight cases reported here, evidence of metastatic involvement of the regional lymph nodes was present in two cases, and evidence of metastatic involvement of the lungs was present in one case. As seven of the patients are living, the ultimate occurrence of metastatic involvement in the entire group is not determinable. It does not seem likely that the distribution of secondary lesions will vary materially from that found in the larger groups, which include patients of all ages.

DIAGNOSIS

It is admitted by all observers that malignant disease of the thyroid gland offers great difficulties in respect to its clinical recognition. It is evident, and also frequently so stated, that correct diagnosis early in the course of the disease is much more rare than at a later time, when the lesion has progressed to the stage at which curative measures for treatment cannot always be employed. In the series of 438 cases, which was reported by Pemberton, an absolute clinical diagnosis was made in 54 per cent, and a presumptive or tentative diagnosis was made in an additional 7 per cent. Thus, in 39 per cent of cases, the clinical diagnosis was either doubtful or incorrect.

In the group of cases reported here, difficulties of diagnosis are evident. One of the most prominent reasons for failure to diagnose carcinoma of the thyroid gland probably is the rarity of the condition in childhood. In Cases 2 and 7 it might justifiably be advanced as an excuse that enlargement of the cervical lymph nodes was the only finding and that involvement of the thyroid gland was not evident. However, in the other cases in which the mass or masses were visible and palpable in the substance of the thyroid gland, conditions other than carcinoma were suspected. Strangely enough, in our experience at the clinic, a large majority of tumorous enlargements of the thyroid glands of children, exclusive of the enlargements which obviously were the result of exophthalmic or simple colloid goiters, have proved to

be malignant. Hence, it would appear that a mass in the thyroid gland of a child, unlike a mass in the thyroid gland of an adult, first should give rise to the suspicion of a malignant lesion.

Another reason for the apparent lack of clinical diagnostic acumen in the cases which are reported here is the fact that in three of them the patient was first seen when the condition was of relatively short duration. In all of the cases the diagnosis was established by microscopic examination of tissue, which was obtained either from the primary tumor or from the regional lymph nodes that were involved. It is therefore of secondary importance that a correct clinical diagnosis was not made, since in each case the true state of affairs was promptly determined and steps were taken to eradicate the disease. It does not appear probable that clinical interpretation alone is sufficient to disclose malignant disease of the thyroid gland. Therefore surgical exploration of the masses in the thyroid gland, or of enlarged cervical lymph nodes, must constitute an essential or integral part of the diagnostic procedure in cases in which there is doubt as to the cause of enlargement.

PATHOLOGY

The recognition and classification of carcinoma of the thyroid gland, according to pathologic criteria, have been controversial. Wilson, in 1921, said that "pathologic diagnosis must take into account the usual development of malignant tumors of the thyroid from proliferating embryonic adenomas." Graham, in 1924, expressed the opinion that "the morphological character of the cells and tissue is an unreliable basis for the determination of malignancy of thyroid epithelial tumors. The malignancy of thyroid epithelial tumors depends upon their tendency or capacity to invade the capsule, surrounding tissue, lymphatics, or blood vessels. The most constant single indication of thyroid epithelial malignancy is invasion of the blood vessels. Scirrhous and papilliferous adenocarcinomata are the only two types of epithelial malignancy in which invasion of the blood vessels has not been observed. These two types together constitute about 51 per cent of the total and are primary lymphatic invaders. Epithelial tumors that are encapsulated and show no invasion of the blood vessels are benign, irrespective of their microscopic appearance otherwise."

The criteria on which the diagnosis of carcinoma is based in this series of cases are those which are accepted generally by pathologists. Briefly, they comprise the evidences of cellular anaplasia and differentiation. Hypertrophy of the nuclei in malignant cells and the resultant disturbance in the nuclear-cytoplasmic ratio are considered of prime significance. It further is to be recognized that in the process of anaplasia, changes take place in the directions of differentiation

as well as in undifferentiation, so that the pathologic picture may include appearances ranging from excessive differentiation to marked undifferentiation. The criteria on which the degree of malignancy has been based are those which have been established by Broders.

PROGNOSIS

The outlook in cases in which carcinoma of the thyroid gland affects children depends on several factors. The degree of malignancy of the tumor would appear to be of prime importance in determining the life expectancy of the patient. If one can judge by the degree of malignancy that was found in the cases in this series, it may be said that carcinoma of the thyroid gland which affects children tends to have a low grade of malignancy. This should be indicative of a slow rate of growth, and metastatic involvement should occur only after a considerable period.

The type of carcinoma also is of great significance in the matter of determining the outlook for life. According to Pemberton, a cure which lasted for three years or longer occurred most frequently in cases in which there was a papillary adenocarcinoma, grade 1 or 2. It occurred next in order of frequency in cases in which there was a malignant adenoma, grade 1, 2, 3, or 4. The least favorable results were obtained in cases in which there was a diffuse carcinoma which was graded 2, 3, or 4. Cures, which lasted for three years or longer, were obtained in 32 per cent of the cases which were reported by Pemberton.

Obviously, the degree of invasion of surrounding tissues and the occurrence of metastatic lesions are determining factors, both in regard to the type of treatment which can be employed and in regard to the ultimate prognosis. Carcinomas which begin as encapsulated growths and which have not extended beyond their enveloping capsules offer the best probability for complete cure. Those starting as encapsulated neoplasms but extending beyond the confines of the capsule, and those which are primarily nonencapsulated and which have invaded surrounding structures and tissue offer great, though as shown by Pemberton not always insurmountable, obstacles to their complete eradication.

A further factor in prognosis is the peculiar radiosensitiveness of carcinomas of the thyroid gland. Although the general rule is that radiosensitiveness increases as the degree of malignancy increases, the carcinomas in the cases which are reported all revealed low grades of malignancy but were rather markedly radiosensitive. This frequently has been mentioned by others, and seems to be a fact which is substantiated by the experience.

It appears, therefore, that, in respect to carcinoma of the thyroid which affects children, there are many factors which favor a desirable outcome; factors which are not present in carcinoma elsewhere in the body. It is probable that these favorable factors, together with adequate treatment, are responsible for the relatively long duration of life in this group of young patients.

The condition is known to have been present for from nine months in Case 7 to twenty-eight years in Case 1. Seven of the patients are known to be alive at present, and they have had the disease for from two to thirteen and a half years. In the one case in which distant (pulmonary) metastatic involvement has taken place, the patient has a moderate degree of disability, but the other patients have been either little incapacitated or have not been incapacitated at all. It has been very striking that in this group of cases, all the carcinomas revealed a low grade of malignancy; in four of the cases the carcinoma was graded 1, and in four cases it was graded 2. All the tumors were adenocarcinomas, and six of them were of the papillary type. Thus, the long period of life in these cases seems to be entirely in agreement with the features of the disease that favor slow growth and invasion, and late metastasis to distant regions.

It is not true that carcinoma of the thyroid gland which affects children always offers such a favorable outlook. In a case reported by Cattell, the carcinoma was of a very malignant type, and death took place sixteen and a half months after the carcinoma first became evident.

TREATMENT

Pemberton has considered methods of treatment and the basis for employing these methods. In early cases in which the carcinoma occurs within an adenoma, and in which the growth is encapsulated, removal of the adenomatous tissue is sufficient. If not encapsulated, the entire lobe containing the growth should be removed. In cases in which there are metastatic lesions, operation should be resorted to, in order to relieve tracheal obstruction when present, and for the removal of the primary lesion and the neighboring nodes in case the carcinoma is of the mild papillary type. All patients should be treated postoperatively with radium which should be inserted into the wound, or applied by means of surface packs. Roentgenotherapy also may be employed. Although the patient may not be seen until the condition is incurable, life may frequently be extended for from two to four years as a result of the insertion of radium needles or the local application of radium.

SUMMARY AND CONCLUSIONS

1. Carcinoma of the thyroid gland is rare among children.

2. Eight cases in which carcinoma of the thyroid gland affected children are reported.

3. The etiologic factors are discussed.

4. The symptoms are such as to account for the fact that correct clinical diagnosis, unaided by microscopic examination, frequently is not made until the process has progressed beyond the stage of complete curability.

5. Metastatic lesions were found to appear infrequently and late.

6. The diagnosis should include examination of tissue, either obtained for biopsy or from the resected portion of the gland.

7. All the carcinomas in this group of cases revealed a low grade of malignancy. This may indicate that low grade malignancy is of more frequent occurrence than high grade malignancy in carcinomas of the thyroid gland, which affect children.

8. Unusually favorable prognosis is frequent in these cases because of the low grade of malignancy, the relatively early institution of treatment, and the radiosensitiveness of the growth.

9. Treatment consists of radiotherapy or of surgical resection combined with radiotherapy.

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CLINICAL ASPECTS OF CHILD DEVELOPMENT RESEARCH

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IT SEEMS almost necessary to begin with a definition. The term "clinic" has medical and even hospital connotations. Etymologically it derives from "bedside." So construed, a clinic is a ward with beds for treatment and teaching. In technical theology the same etymology holds. Clinical baptism is a bedside baptism which comes at the end of the life career, at the sick bed or deathbed. But in modern days the term "clinical" has lost some of these associations, and without blinking, one can use such an expression as a "well baby clinic."

The term "clinic" now suggests a laboratory and other facilities for examination, consultation, supervision, and treatment. Of course, the term may be used so loosely that it preserves no distinctive meaning. In the present discussion it scarcely serves any purpose at all unless it denotes a medical type of organization, and in that sense I shall use the word.

Now if we look into the history of modern clinical medicine, we shall find that the fundamental functions of a clinic are much alike. They include: (1) diagnosis, (2) treatment, and (3) investigation. In an ideal clinic these functions are vitally and extensively related. Individual clinics differ enormously in origin and in details of organization. In a somewhat individualistic manner they tend to embody the ideas of a single person or a group of persons, and they have their roots in peculiar local conditions. Clinics also freely undergo shifts of organization in response to new medical discoveries. Such variations and flexibility are desirable. It is impossible even in a large medical center to give equal weight and representation to each and every division of medicine.

The relationship which child development will have to any clinical set-up will, therefore, naturally depend upon personal and historical factors. It would be rather useless to outline an ideal organization particularly in a field so diverse and protean and lacking in tradition. Child development, however, has so many actual and potential relationships with medical science and clinical medicine that we may consider briefly a few fundamental principles which underlie the whole problem of research organization and research coordination.

What is the status of child development when envisaged in terms of medical research and medical service? For the purpose of practical

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Based on a paper read at the First Biennial Meeting of the Society for Research in Child Development at Washington, D. C.

delimitation, I shall pass over the special problems which arise out of the interrelations between child development and the social sciences. It is convenient to consider child development as a branch of human biology. Child development then becomes a focal field for psychobiologic and medical knowledge, converging upon the central problems of human growth. Even when so delimited, this represents a prodigiously inclusive field of inquiry.

So defined, child development has its major roots in four great scientific disciplines, namely: (1) anatomy (including physical anthropology), (2) biochemistry, (3) physiology, and (4) psychology. It is interesting to note that the quarterly *Child Development Abstracts,* a publication edited by the Committee on Child Development, draws its material from fifteen different journals.* Easily half of these are medical in character.

The modern medical center, which is one of the striking developments of the last decade, is arranged to centralize as nearly as possible the activity of medical staff members and investigators in the fundamental sciences. Hospital wards, dispensaries, teaching laboratories, research laboratories, and examining rooms adjoin each other horizontally and vertically. Individual specialized clinics are legion and range from allergy to radiology and dental surgery. The research activities of these clinics have direct relationships to the scientific growth of child development. It is obvious, therefore, that any child development research unit which is architecturally and functionally closely related to such a medical organization will inevitably benefit from juxtapositions and from currents of cross-fertilization.

Although in its internal organization the medical center shows many evidences of increasing specialization, there are counteracting influences which prevent this specialization from becoming disintegration. There is at present, both in teaching and in practice, a strong trend toward a recognition of the unity and indivisibility of the individual. Child development as a scientific movement stands for a similar concept and will doubtless make contributions toward the realization of the concept.

If this analysis is sound, it follows that child development research should in principle associate itself with those trends and forces which have been gathering strength and form throughout centuries of medical progress. This argument leads to another consideration.

With what field of medicine is child development most fundamentally identified? From many points of view, it must be the field of pediatrics. Pediatrics holds a unique place in the whole scheme of medicine and of public health. Pediatrics is a specialty and yet it is not a specialty.

*(1) The Journal of the American Medical Association, (2) The Wistar Institute Biographic Service, (3) American Journal of Physical Anthropology, (4) The Journal of Nervous and Mental Disease, (5) American Journal of Diseases of Children, (6) The Journal of Bone and Joint Surgery, (7) Archives of Neurology and Psychiatry, (8) Nutrition Abstracts and Reviews, (9) Journal of Home Economics, (10) Psychological Abstracts, (11) Physiological Abstracts, (12) Biological Abstracts, (13) Chemical Abstracts, (14) Mental Hygiene, (15) Endocrinology.

It is concerned with a sector of life (rather than a subdivision of the organism)—the same sector with which child development research has been peculiarly concerned. Most of the specialties in medicine deal with some particular function or structure of the body—the eyes, ears, nose, throat, nervous system, etc. Pediatrics, however, is concerned with the infant or child as a whole; it remains, as Osler called it, "the specialty of general medicine."

Pediatrics holds a peculiarly strategic position representing the integration of the resources of general medicine in the health protection of normal as well as of sick infants. In the next few decades research in the biologic sciences (including child development) will doubtless provide new and discriminating technics for the measurement and clinical appraisal of human characteristics, mental and physical. Such technics will define with greater precision individual differences in body build, constitutional type, biochemical susceptibilities, physiologic efficiencies of separate organs, and above all behavior traits and trends—the balance and correlation of functions in the total personality.

A clinical type of organization places child development in a position where it can align itself with these fundamental medical trends. A clinical organization makes possible intimate contact with diagnostic problems which come to associated clinics. Although it is possible to organize a clinic on a purely research basis, we may well believe that in general the most promising type of organization recognizes the three fundamental functions of (1) diagnosis, (2) treatment, and (3) investigation. This type of organization in no sense precludes work with so-called normal children. The trend of medicine is so strongly preventive that it will place increasing premium upon supervisory forms of control which can be best exercised by means of a clinical organization and which will reach all groups of humanity whether normal, sick, or defective. The clinical investigation of individual cases and the application of knowledge in the study and treatment of *individuals* will be in the future, as in the past, indispensable to medical progress.

SUMMARY

I have purposely dealt with the broader considerations which underlie the medical aspects of child development research, for general principles, if they are sound, must have major weight in the long-range projection of research plans.

The scientific advantages which come from a clinical type of organization may be summed up as follows:

1. A diagnostic and advisory clinical service as a basic part of a research unit brings the unit into natural working relations with parents and with community agencies.

2. Such a service, dealing both with normal and exceptional children, helps to disclose significant cases and trends which repay intensive developmental study and clinical research.

3. Such a service leads to the accumulation of consecutive records over a period of years. It favors biogenetic studies.

4. Close working relationships with associated clinics favor coordinated effort and a correlation of developmental data.

5. Increased accessibility to the technical resources of the basic sciences of anatomy, physiology, and biochemistry facilitates investigation in these fields with special reference to problems of child development.

6. A clinical orientation can promote investigation and experimental demonstration of procedures which may be used in the developmental supervision of infants and preschool children; and in the management of children who need special care, including ill, convalescent, and handicapped children.

7. Finally, a clinical type of organization fosters assimilation with the existing agencies for the study and protection of normal development. It is in harmony with the integrating trends of clinical pediatrics and of medical research in general.

STANDARDS OF BASAL METABOLISM OF GIRLS (NEW DATA) AND THEIR USE IN CLINICAL PRACTICE

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THE first observations of the basal metabolism of children were made in physiologic laboratories and required such a difficult and complicated technic that the number of cases studied was limited. After several years sufficient data was obtained so that the metabolism of young normal children could be predicted with accuracy. Various standards were devised and used with considerable success in clinical practice. The development of the portable apparatus by Dr. Francis G. Benedict made it possible for hospitals and clinicians to obtain the metabolism of a large number of patients over eight years old, and, as a result, a tremendous amount of literature on basal metabolism developed.

It became common practice to express results of metabolism determinations in terms of plus or minus variation from some standard of metabolism. Various standards and formulas were devised and very satisfactory results were obtained for adults and also for children of average build and development. Difficulties arose, however, when these standards were used for children of abnormal physical status, which represents the group in which accurate data in making a diagnosis was most essential. This was due in part to the fact that enough normal data had not been obtained for children between the ages of ten and twenty years and, in part, to the fact that standards in common use do not give uniformly consistent results in the abnormal group.

The fact that there was insufficient material on which to base standards between the ages of ten and twenty years made it essential to obtain more inclusive standards for all ages. With this in view, the metabolism of a new series of 120 girls in a private school in Boston was obtained; eighty-seven of these had the average normal physical development (between minus 9 and plus 20 per cent weight for height, Baldwin-Wood standard) and were used in this report.

It became clear that mathematics alone could not solve the problem. It can and does tell which standard shows the smallest mathematical variation in average normal children, but it does not tell which gives the most accurate estimation of the clinical status of the pathologic child. With this in view, one of us has made it a practice for the past ten years to estimate the variation in metabolism of each

pathologic case by as many standards as possible for the purpose of finding which standard gave results which corresponded with clinical experience and use of which resulted in the fewest clinical errors. The standards which are presented here were developed in two ways; first, to agree with clinical experience; and second, to be reasonable mathematically. The standards given are not presented as the last word because the data are still being studied from new angles. They are presented as standards which today seem to result in more accurate clinical diagnosis than other standards. It is not inconceivable that they may be modified as the work progresses.

That there is a sharp dividing line between the methods used in physiologic laboratories and in clinical office and hospital practice should be understood by everyone who makes metabolism studies. In the former instance, it is usually possible to control and eliminate everything that affects the basality of the metabolism; whereas in the latter conditions are less easily controlled. In the former, those who do the work are familiar with the literature of the subject and know all the factors which influence the metabolism, while in the latter dependence is placed too often on interpretations by technicians who may have had only a week's special training. I have seen many original kymograph drum records on which were based reports in the literature which never should have been reported as *basal periods*. It is possible, however, for a clinician to take precautions which will eliminate most of the errors.

Since a large number of observations on girls were needed to obtain enough data to fill in the gap between the ages of ten and twenty years, it was necessary to collect this series in a manner similar to that used in clinical practice. The same care that was used in the physiologic laboratory was attempted here, but, on account of physical difficulties and the character of the subjects, it was felt that this series represented a clinical rather than a physiologic research. It was felt also that as these data were to be compared with other clinical data obtained by a similar technic, it was peculiarly fitted to the purpose.

The material used was a group of private school girls who belonged to a socially and economically fortunate level of the population. Physically they were all healthy, and their growth and development was good. Only those girls whose weight for height fell within minus 9 and plus 20 per cent of the Baldwin-Wood standard were accepted. The younger group, taken from the earlier work of Benedict and Talbot,[1] was selected in the same manner. These children came from the less fortunate part of the population, but they also were physically healthy.

It was found that although various standards could be constructed, such as surface area and height-weight relationship, they did not meet the needs of the large group of cases with abnormal body build, especially with variations in the height-weight ratios which are common in clinical practice. It had previously been found that fewer errors in diagnosis resulted, and a more accurate clinical picture was obtained if the metabolism of children was compared with the total calories for the height and the total calories for the weight. These are presented in Table I.

These tables were obtained from the data furnished for 179 girls by graduating in accordance with Whittaker's method (E. T. Whittaker and G. Robinson, *Calculus of Observations*, p. 303) as follows: The logarithms of the weights were divided into 14 equal groups, and the mean logarithms of the calories were figured for the groups as centered at the midpoint of the group; these 14 means (equally weighted although the number of data entering into the means varied) were graduated by the method using $\epsilon = 0.01$ as the value of the adjustable parameter; the graduation for calories against height was similar with 12 means and $\epsilon = 0.05$. Interpolation to second differences was applied to the logarithms of the calories as graduated, and the logarithms were then converted into calories. Logarithms were used because it is the percentage variation rather than the actual variation in calories which is more or less regular over the wide range of data.

Curves for heat production for both height and weight were constructed, and it was found that in general the standards underestimate the calories at about one year of age and between eleven and thirteen years, and overestimate them from three to eight years and from seventeen years on. Because of the small number of cases, it is impossible to say whether or not this age effect is significant.

Actual count shows that two-thirds of the group fall within 12 per cent plus or minus of the standards. The balance are more than 12 per cent above or below, and 5 per cent are more than 25 per cent above or below the standards. As such variation is a necessary corollary of the essentially statistical nature of the problem, it illustrates in a striking manner the danger of accepting literally any standard. It is interesting to notice that if a girl has a high metabolism rate when the weight standard is used for production she also has a high metabolism when the height standard is used. Averaging the two values of the metabolic rate, therefore, makes little difference since they are essentially the same. We have tried to find reasons for this variation, but so far we have had very little success. Apparently people who are high in calories are high in calories. We cannot emphasize too strongly the importance of balancing all other available clinical data in making interpretations from metabolism findings.

It is unnecessary here again to emphasize the importance of obtaining basal figures in the first case. All possible precautions were taken both in this work and in the series reported by Benedict and Talbot.[1] In the new series a large number of observations were dis-

TABLE I

STANDARD TOTAL CALORIES FOR WEIGHT AND TOTAL CALORIES FOR HEIGHT—GIRLS (BENEDICT AND TALBOT AND TALBOT PRIVATE SCHOOL GIRLS)*

WEIGHT (KG.)	TOTAL CALORIES PER 24 HOURS	HEIGHT (CM.)	TOTAL CALORIES PER 24 HOURS
3.0	136	48	134
4.0	205	50	159
5.0	274	52	186
6.0	336	54	214
7.0	395	56	246
8.0	448	58	278
9.0	496	60	309
10.0	541	62	341
11.0	582	64	373
12.0	620	66	404
13.0	655	68	433
14.0	687	70	462
15.0	718	72	489
16.0	747	74	515
17.0	775	76	539
18.0	802	78	560
19.0	827	80	581
20.0	852	82	601
22.0	898	84	619
24.0	942	86	636
26.0	984	88	652
28.0	1,025	90	666
30.0	1,063	92	681
32.0	1,101	94	695
34.0	1,137	96	709
36.0	1,173	98	722
38.0	1,207	100	735
40.0	1,241	105	770
42.0	1,274	110	807
44.0	1,306	115	846
46.0	1,338	120	894
48.0	1,369	125	942
50.0	1,399	130	987
52.0	1,429	135	1,057
54.0	1,458	140	1,130
56.0	1,487	145	1,208
58.0	1,516	150	1,294
60.0	1,544	155	1,386
62.0	1,572	160	1,477
64.0	1,599	165	1,544
66.0	1,626	170	1,584
68.0	1,653	175	1,596
70.0	1,679	180	1,600†
72.0	1,705	---	----
74.0	1,731	---	----
76.0	1,756	---	----
78.0	1,781	---	----
80.0	1,805	---	----

*Obtained entirely in cot chamber, 3.0 to 32.0 kg. 48 to 130 cm.; part cot chamber and part portable apparatus 34.0 to 40.0 kg., 135 to 150 cm.; entirely with portable apparatus 42.0 kg. and above, 150 cm. and above.

†Work that we are doing on cases collected from the works of other investigators indicates that the upper figures in the height standard may have to be modified.

carded because they did not fulfill basal requirements. When one considers the care with which this data was collected and the fact that neither the physician, the school, nor the registered nurse,* who examined the girls just before the test, was able to detect anything abnormal about them, it shows how much latitude of interpretation must be taken in clinical practice.

A discrepancy seen in some of the curves between the upper end of the younger Benedict and Talbot group and the lower end of the new series finds a possible explanation in the fact that the metabolism rate of the former was obtained in the cot chamber and that of the latter by means of the Benedict-Roth portable apparatus.†

The literature has been searched for all records of basal metabolism of normal girls. We have corresponded with all the authors quoted here and received the greatest help and cooperation. We also have data from other authors which is not included because their series were not sufficiently large to be treated separately. These data will be included in another report. Many of the authors went to much trouble in supplying us with the total calories which were not published in their original articles, and others have entrusted us with unpublished data. We wish to express our appreciation for their kindness and cooperation, especially to Dr. Marion E. Stark, of the University of Wisconsin.

In this connection we emphasize the importance of publishing in all cases, whether single cases or groups, normal or pathologic, the total calories produced without which the data is worthless. The plus or minus variation of metabolism may also be reported, but it should be accompanied by a statement of which standard is used for comparison.

The series recorded by various authors were put through the same mathematical analysis as ours, and their variation from the Boston groups recorded in Table II.

The heat production of children of the same ages was compared, and it was found that the results of various observers were not uniform. The metabolism of older girls studied by Coons,[3] Tilt,[11] Remington and Culp,[7] and Stark[9] was considerably lower than that of the Boston and California[4] girls. These comparisons make it obvious that, if a standard made up of a single group of figures is to be used, it must be corrected if used elsewhere for the characteristics of the group. This is consistent with the experience of Cameron of Winnipeg (personal communication).

The use of similar standards in clinical practice has been discussed in an earlier paper,[10] and nothing has developed in this investigation which changes the general conclusion that comparing the metabolism

*Miss Ebba C. Blomquist, R. N.

†Kindly supplied by Warren E. Collins, Inc.

TABLE II

COMPARISON OF HEAT PRODUCTION RECORDED BY DIFFERENT OBSERVERS

OBSERVER	AGE (YR.)	NUMBER OF CASES	DEVIATION	
			TOTAL CAL. FOR HEIGHT (%)	TOTAL CAL. FOR WEIGHT (%)
Benedict and Talbot (Boston)	0-13 incl.	92	0	0
Talbot (New Series Private School) (Boston)	10-19 incl.	87	0	0
Lucas (San Francisco, Calif.)	8-18 incl.	207	− 1	− 1
Stark (Hospital cases) (Wisconsin)	9-16 incl.	52	− 4	− 2
MacLeod (New York)	10-15 incl.	56	− 2	+ 1
Topper (New York)	10-16 incl.	39	+ 4	+ 4
Blunt (Chicago)	8-17 incl.	58	+ 4	+ 3
McKay (Ohio)	13-18 incl.	80	− 8	− 7
Stark (University students) (Wisconsin)	17-20 incl.	86	−15	−12*
Remington and Culp (South Carolina)	18-20 incl.	37	−13	−10*
Coons (Oklahoma)	17-22 incl.	99	−17	−16*
Tilt (Florida)	17-20 incl.	40	−16	−14*

*In these four groups the lower limit of age is at the figure (seventeen years) beyond which we suspect that our standards may be too high.

with the total calories for the height and the total calories for the weight leads to fewer clinical errors in individuals with abnormal development, especially variations in the height-weight ratio than other standards. Since the standards which make corrections for these factors and also age should be more accurate mathematically but are not even with normal children, there is no advantage in using them even for the normal.

SUMMARY

1. The metabolism of a new series of eighty-seven normal girls between the ages of ten and twenty years with exceptional economic advantages was obtained. These data were combined with that which had previously been reported by Benedict and Talbot to enlarge and modify their standards. These standards are presented.

2. It was found that the percentage deviation in normal girls may be more than plus or minus 12 per cent above or below the standards given in one-third of the cases. Therefore, too much emphasis should not be laid on minor variations outside the commonly used plus or minus 10 per cent limit.

3. Variations of between minus 12 and minus 20 per cent are receiving special study; those at the lower limit may be significant while those of less than 17 per cent probably are not.

4. Variations of more than minus or plus 20 per cent are probably significant when there is no doubt of the basality of the figures. There are indications that the progress of this study may reveal exceptions which will make an even closer correlation possible.

5. Finally, if these standards are used in other regions, they should be adjusted to the characteristics of the group of that region.

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DIPHTHERIA IMMUNIZATION

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IN ELEVEN years' experience (1924-1935) with diphtheria immunization in the Los Angeles City Health Department, we have had an opportunity to observe the different immunizing agents, the reactions produced by them, the relative immunity established, and the opportunity of completing the immunization when more than one injection is necessary.

From the beginning of diphtheria immunization by the Los Angeles City Health Department in 1924 until March, 1935, we have immunized approximately 84,575; of these, 46,616 with toxin anti-toxin, 35,946 with plain toxoid, and 2,013 with alum-precipitated toxoid.

Our experience undoubtedly corroborates the findings of other health departments in that many children do not complete their full course of immunization if more than one injection is needed. It is readily understood that with this fact in mind we were gratified to read in the literature that a one-dose toxoid was available. Past experience, however, had shown us that we must be very cautious in introducing a new immunizing agent. In a previous paper[1] we showed that, when we first began the use of toxoid (Ramon) to replace toxin anti-toxin, we had some rather severe reactions and considerable objections from school groups. However, this difficulty was overcome as the toxoid became better refined and the reactions became less severe. For the past two years we have limited ourselves to toxoid and discontinued the use of toxin anti-toxin. Toxoid enabled us to produce better immunity in a shorter time with fewer injections, and eliminated the possibility of serum sensitization.

Recent observations reported on alum-precipitated toxoid seemed to indicate that a still better immunizing agent was available.

Apropos to the development of a one-dose toxoid were Glenny's observations that the addition of alum to toxoid increased appreciably its power to develop anti-toxin when injected in horses. Following this, Park and Schroder[2] advantageously used toxoid to which 0.2 per cent alum had been added in the immunization of some infants and children. The increased efficiency of alum toxoid was attributed to lessened solubility of the toxoid and correspondingly slow absorption.

In 1931 Glenny and Barr[3] described a method of complete precipi-

From the Los Angeles City Health Department.
Read at the Pediatrics Section of the California State Medical Meeting at Yosemite, May 13, 1935.

tation of toxoid by the use of alum. They pointed out that because of its slow absorption alum toxoid remained in the body long enough to act as its own secondary stimulus. Later, Wells, Graham, and Havens,[4] of the Alabama State Health Department, obtained a purified product by complete precipitation of toxoid with aluminum potassium sulphate. They used one injection of 1 c.c. of their precipitated toxoid on a group of ninety-eight children who were known to be Schick positive, and eight weeks later they found 94 per cent of these Schick negative.

Graham, Murphree, and Gill[5] reported observations on 798 children. In a group of 185 strongly Schick-positive children, 171 (92.4 per cent) became Schick negative. In a group of 613 whose immunity status was unknown, 592 (96.6 per cent) were Schick negative two to four months after a single injection.

We were so favorably impressed by the clinical reports that we decided to try some alum-precipitated toxoid at our conferences. We were cautious in our first attempts, starting with small groups of no more than ten at a time. These were carefully checked within twenty-four and forty-eight hours by home visits by a public health nurse.

Observations were made on both local and general reactions. Under local reactions we noted the extent of involvement around the area of injection: redness, swelling, soreness and tenderness, induration, nodule formation, and central softening. Under general reaction, we noted temperature, general malaise, headache, nausea, or vomiting. Results reported were so favorable, reactions so negligible, that, after observing about sixty in this manner, we decided to proceed more rapidly in the use of alum-precipitated toxoid in our immunization work. The first group observed was limited to a preschool conference group, ages ranging from six months to six years. Our next step was to immunize two small school groups, from six years to ten years of age, also with gratifying results. Following this we scheduled several larger schools for one-dose alum precipitated toxoid.

It was at this time that we noted some observations at variance with our initial observations. A school nurse reported severe reactions and loss of time from school; the school principal was panicky. This was two weeks after the toxoid was given. I went to the school and observed 171 children who had been immunized and found that there was cause for alarm. Thirty marked local reactions and eight abscesses, six of which had ruptured spontaneously and two of which had been lanced, were noted. We thought possibly the toxoid from one manufacturer of biologic products might be giving bad results, so we tried other brands. Our results did not vary much.

In order to make closer observations at the conferences, all mothers were told to return within one week. We found more severe reac-

tions than we had expected; certainly not the favorable results reported by our nurses. It was evident that at the end of twenty-four, forty-eight, or even seventy-two hours reactions were no more marked than with ordinary toxoid, or even less marked. At the end of one week or ten days the picture changed—in a number of cases abscesses developed. We had an opportunity to incise and make cultures from two such abscesses—they were sterile. In other cases we observed them after they had ruptured spontaneously or after they had been incised by doctors in private practice, and no cultures were taken. In a group of 1,360 children who were given alum-precipitated toxoid, seventeen abscesses, which either ruptured spontaneously or were incised, were observed, and, in addition, more than twice that number were characterized by central softening, i.e., tissue changes. The most severe reactions were observed in children over six years of age. It is not surprising that at this time we decided it was best to discontinue the use of alum-precipitated toxoid until further refinement of the product.

It was not long after this that the National Institute of Health standardized the percentage of alum in the product not to exceed 20 mg. per human dose, and it was generally considered that results would be more favorable. The literature continued with favorable reports.

McGinnes, Stebbins, and Hart,[6] of Virginia, reported on 1,765 Schick-positive cases, 94.4 per cent of whom were rendered Schick negative in two months, and 347 cases, 95.1 per cent of whom were rendered Schick negative at the end of one year with 0.5 c.c. alum-precipitated toxoid. In 3,000 cases only one abscess developed. In only one lot of alum-precipitated toxoid used in Virginia a high percentage of abscesses, 12 in 112 individuals, came to their attention.

Baker and Gill[7] reported 100 per cent immunity in 197 Schick-positive children with a single injection of 1 c.c. of precipitated toxoid and 99 per cent immunity, two to three months later, in 1,414 whose Schick reactions were not taken. Observations on 16,289 inoculations revealed eight abscesses. Local or general reactions were not severe.

McGinnes and Stebbins[8] reported 95 per cent immunity in a group of 579 previously Schick-positive individuals within six to nine weeks after 0.5 or 1 c.c. alum-precipitated toxoid was given. The immunity produced with one-dose alum-precipitated toxoid compared favorably with two doses of plain toxoid. No untoward results were reported.

Walker,[9] of Alabama, reported 100 per cent negative Schick tests within two to six months in 1,924 children ranging in age from under one year to twelve years whose immunity status was not known and in 165 children who were originally Schick positive.

Impressed by these favorable reports we began observations on a second series of alum-precipitated toxoid about six months after our first observations. In this series we used six different brands. The amount of alum per dose in these brands conformed to standardization by the National Institute of Health, ranging between 10 to 20 mg. per human dose. On the whole, this was considerably less alum per dose than contained in our first series.

The results in this series were much better than in the first; abscess formation was considerably less marked. In a group of 653 children ranging in age between six months and ten years, we had two (presumably sterile) abscesses with drainage and six without drainage which healed by absorption. All these abscesses were observed in children over five years of age. We also noted twenty-nine tissue changes which were characterized by central softening but which did not advance to abscess formation. Twelve of such tissue changes were in children of school age and seventeen in a preschool group. General reactions were not any more marked than with plain toxoid. A factor which caused concern to parents was the persistent indurated nodule which ranged in diameter from 1 to 2 centimeters. In this series, also, we felt that we did not altogether favor the alum-precipitated toxoid, especially in older children. Even an occasional abscess is undesirable.

The primary factor in evaluating an immunizing agent is its immunizing power. In our first series in a group of 175 children who were known to be Schick positive, 160, or 91.4 per cent, gave negative Schick reactions within six weeks to three months after the alum-precipitated toxoid was given (Table I).

TABLE I

ALUM PRECIPITATED TOXOID, SERIES 1

INITIAL SCHICK POSITIVE	RECHECK BY SCHICK TEST 6 WK. TO 3 MO. LATER	
	NEGATIVE	POSITIVE
175	160 91.4%	15 8.6%

In our second series we compared six different brands of alum-precipitated toxoid. In a group of 335 who were known to be strongly Schick positive, we obtained 289, or 86.3 per cent negative Schick reactions, 24, or 7.2 per cent slightly positive, and 22, or 6.5 per cent positive within eight to nine weeks after immunization. In this same group an additional 51 whose previous immunity status was not known when tested eight to nine weeks later gave us 44, or 86.3 per cent negative, 4, or 7.8 per cent slightly positive, and 3, or 5.9 per cent positive (Table II). We believe those slightly positive may become Schick negative a little later. However, there is likewise the possibility that there may be a reversion of a small percentage of those

Schick negative to the Schick-positive stage, as brought out by McGinnes, Stebbins, and Hart,[6] and also by Volk.[10]

TABLE II

ALUM PRECIPITATED TOXOID, SERIES 2

BRAND	INITIAL SCHICK POSITIVE	SCHICK TEST 8-9 WK. AFTER IMMUNIZATION		
		NEGATIVE	SLIGHTLY POSITIVE	POSITIVE
Brand 1 1.0 c.c. dose	104	84 80.8%	9 8.6%	11 10.6%
Brand 2 0.5 c.c., 1.0 c.c. dose	39	37 94.8%	1 2.6%	1 2.6%
Brand 3 1.0 c.c. dose	37	34 91.9%	0	3 8.1%
Brand 4 0.5 c.c. dose	45	41 91.1%	3 6.7 %	1 2.2%
Brand 5 0.5 c.c. dose	32	25 78.1%	5 15.6%	2 6.3%
Brand 6 1.0 c.c. dose	78	68 87.2%	6 7.7%	4 5.1%
All brands	335	289 86.3%	24 7.2%	22 6.5%
	Immunity status not known			
All brands	51	44 86.3%	4 7.8%	3 5.9%

We compared these results with immunity established with other immunizing agents used by us. In a group of 1,168 children whose immunity status was unknown, three injections of 1 c.c. toxin anti-toxin rendered 1,027, or 87.9 per cent negative within six months to one year. In a group of 1,070 children whose immunity status was likewise unknown, two injections of 1 c.c. toxoid rendered 1,005, or 94 per cent negative within six months to one year. In our alum-precipitated group we had 91.4 per cent immunity within six weeks to three months in one series and 86.3 per cent immunity within eight to nine weeks in a second series. This group includes both those known to be Schick positive and those whose immunity status was unknown prior to immunization. In this later series, however, we feel that the percentage rendered immune will undoubtedly be increased to a higher figure a little later, if we are correct in our interpretation that those slightly positive may become Schick negative.

For comparison we also immunized a group of 139 children (aged six months to ten years), who were known to be Schick positive, with two injections, 1 c.c. each, of plain toxoid, given at two weeks interval.

When their Schick reactions were taken eight to nine weeks after the second injection, we found 96, or 69.1 per cent, negative, 13, or 9.3 per cent slightly positive, and 30, or 21.6 per cent positive. These results were out of keeping with any previous observations made at our conferences with plain toxoid. It is hard to explain these results except, perhaps, that they may turn Schick negative later, or that the toxoid used in this group was not up to its usual potency (Table III).

TABLE III

COMPARISON OF RELATIVE IMMUNITY WITH DIFFERENT IMMUNIZING AGENTS

IMMUNIZING AGENT	NUMBER IMMUNIZED	IMMUNITY STATUS PRIOR TO IMMUNIZATION	TIME AFTER IMMUNIZATION SCHICK TEST DONE	NEGATIVE	SLIGHTLY POSITIVE	POSITIVE
Toxin-antitoxin 3 injections	1,168	Not known	6 mo. to 1 yr.	1,027 87.9%		144 12.1%
Toxoid (plain) 2 injections	1,070	Not known	6 mo. to 1 yr.	1,005 94.0%		65 6.0%
Alum ppt. toxoid Series 1 1 injection	175	Positive	6 wk. to 3 mo.	160 91.4%		15 8.6%
Alum ppt. toxoid Series 2 1 injection	335 51	Positive Not known	8 wk. to 9 wk.	333 86.3%	28 7.5%	25 6.2%
Toxoid (plain) 2 injections	139	Positive	8 wk. to 9 wk.	96 69.1%	13 9.3%	30 21.6%

CONCLUSION AND SUMMARY

1. A review of diphtheria immunization for a period of eleven years by the Los Angeles City Health Department has been presented.

2. A report has been made of immunization with alum-precipitated toxoid in two different series; 1,360 in one group with seventeen (presumably sterile) abscesses with drainage and 653 in another group with two (presumably sterile) abscesses with drainage. Tendency to abscess formation was greater in children over five years of age while central softening was more frequent in children under five years. In Group I in 175 children who were known to be strongly Schick positive, 91.4 per cent immunity, as determined by the Schick test, was obtained within six weeks to three months. In Group II in 335 cases, also known to be strongly Schick positive, 86.3 per cent immunity was obtained within eight to nine weeks, and 7.2 per cent more were only slightly positive. The latter would probably be Schick negative if a longer interval had elapsed. In 51 children whose Schick reactions were not known, 86.3 per cent immunity was obtained and 7.8 per cent more were only slightly positive.

3. Comparison was made of relative immunity with toxin anti-toxin, toxoid, and alum-precipitated toxoid. Our highest percentage of im-

munity was obtained within six months to one year after the injections of two doses of plain toxoid. In a comparative series of plain toxoid and alum-precipitated toxoid a higher percentage of immunity was obtained with the alum-precipitated toxoid within a period of eight to nine weeks after the injections. This probably speaks for alum-precipitated toxoid when quicker immunity is desired.

4. The relative frequency of abscess formation in children over five years of age following alum-precipitated toxoid makes it questionable whether it can be accepted as the sole immunizing agent at present. We feel, however, that in time this factor may be minimized.

NOTE.—Since this paper was written alum-precipitated toxoid was used in several other schools. In one school group in which 123 children were immunized six abscesses requiring incision were formed. These were followed by considerable drainage. Cultures made from two of these abscesses did not show growth on nutrient agar, blood agar, or nutrient bouillon, even after forty-eight hours' incubation.

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116 WEST TEMPLE STREET

SUPRARENAL ATROPHY

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ADDISON'S disease, due to atrophy of the suprarenal glands, is a relatively uncommon condition. The following is the report of a case in a nine and one-half-year-old boy. A discussion of the available literature is included:

A. M., male, was admitted to the Hospital for Sick Children on Dec. 29, 1933, at the age of nine and one-half years, having been referred to the hospital by a local physician because of chorea. The parents related that the boy had been well until one month prior to admission when he developed a cold in the head. He became nauseated, began vomiting, felt weak, lost interest in things, had a pain in the right lower chest, and was short of breath on mild exercise. Further questioning revealed that the boy, who, unknown to him, was adopted, had had frequent bilious attacks all his life. These possibly were imitative in that the foster mother suffered from migraine and bilious attacks about every three weeks. The former attacks had not been severe, and except for these the child had been perfectly well until three or four weeks before the first admission—as the father stated, "He liked to fight and could lick any boy on the street." At that time they observed that he would not play outside but came home from school and lay down. He became weaker and more listless, and anorexia came on during this period. It was also observed just prior to the onset of the illness that the boy was using a large amount of salt from the table. Because of this the mother put the salt out of his reach. His symptoms rapidly became worse when this was done.

Physical examination on admission revealed an emaciated boy who was emotionally unstable. The skin was dry but otherwise normal. The tonsils were diseased; nothing abnormal was found in the respiratory or circulatory systems; the abdomen was scaphoid. There was no evidence of chorea, but there was muscular weakness.

For the first two days there was no change in the child's condition. He was given fluids and a soft diet. There was no vomiting. On Dec. 31, 1933, he began to vomit and had deep sighing respirations; the urine contained a large amount of acetone. The temperature was subnormal. A continuous intravenous injection of 5 per cent glucose in saline was started. The vomiting continued, and the surgical and neurologic staffs were consulted regarding the possibilities of intracranial or intra-abdominal cause for the vomiting. No cause was found. There was some improvement in the next two days, but the acidosis and vomiting continued, though not so marked. Because of the development of phlebitis, the intravenous glucose in saline was discontinued, and parenteral fluids were administered by hypodermoclysis. During the night of Jan. 3, 1934, the child collapsed, became pulseless, and appeared moribund. There was a strong acetone odor to the breath, and there was also acetonuria. Because the usual acidosis secondary to infection or cyclic vomiting is relieved by the therapy that had been administered, it was considered that there must be some other underlying cause of the continuing state and the sudden collapse. The boy had the appearance of general circulatory failure. The systolic blood pressure was found to be 60 mm. of mercury. The diastolic

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pressure could not be recorded. A tentative diagnosis of suprarenal insufficiency was made. A second continuous intravenous injection of 5 per cent glucose in normal saline was started and 5 to 8 minims of a 1:1,000 solution of adrenalin were given intravenously every hour. The temperature and blood pressure rose to normal, and the child improved perceptibly. A roentgenogram taken of the chest in the interval when the intravenous injection was not running showed the heart to be very small (Fig. 1). The vomiting stopped, but the boy would not eat, and the acetonuria continued. The second vein developed phlebitis, and again the intravenous injection of glucose in saline had to be discontinued. Hypodermoclysis was continued, and adrenalin was administered hypodermically at frequent intervals. The general condition remained unchanged with marked anorexia. A glucose tol-

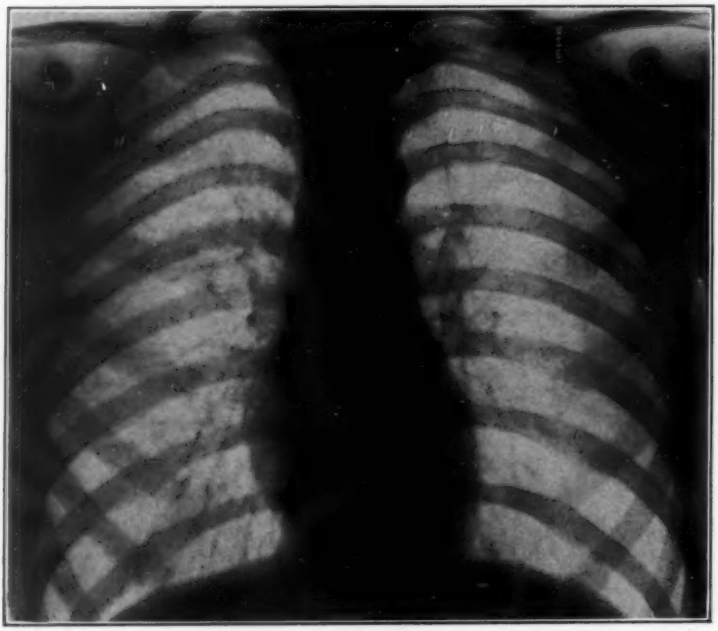

Fig. 1.—Roentgenogram showing the degree of microcardia.

erance test showed a prolonged curve which failed to return to the original in three hours. The tuberculin and Wassermann tests were negative. The patient was removed from hospital against advice on Jan. 12, 1934.

The child was readmitted Jan. 21, 1934, in a state of collapse similar to the one described above. The temperature was 94° F.; he was pulseless, very toxic and dehydrated, and the blood pressure was 65/50.

While in the hospital during the second admission he was treated by transfusion, continuous intravenous administration of glucose and saline, and adrenalin, with periods of improvement and relapse. Later sodium chloride in capsules was offered but refused. An intravenous injection of 100 c.c. of 10 per cent sodium chloride was given with marked improvement. He began to eat and brightened considerably though the emaciation continued. The diet during this period was high in calories and low in fats with 8 gm. of sodium chloride added per day. Salt was

also placed at the bedside, and it was taken in large quantities in buttermilk. He was eating moderately well during this period though he lapsed every fourth or fifth day. He was revived by the injection of saline by hypodermoclysis or intravenously. On Feb. 8, 1934, pigmentation of the abdomen about the interstitial marks was observed (Fig. 2).

On Mar. 2, 1934, the child ate his breakfast and seemed quite bright. One hour later he had a convulsive seizure, became comatose, had more convulsive seizures, and died later in the day. At postmortem the following findings were noted:

Fig. 2.—Photograph of patient taken sixteen days before death. Note the pigmentation.

The body was that of an extremely emaciated white male child about nine years old, 4 ft. 5 in. (135 cm.) tall. The head was covered with a luxuriant growth of dark brown hair, except in the occipital region where much of the hair had apparently been rubbed off. The eyes were somewhat sunken. The abdomen was scaphoid. The skin over the entire body was dry and scaly and of a light brownish color.

This pigmentation was more noticeable around the waist, loins, and back. There were old transfusion wounds in each anticubital fossa and over each internal malleolus; these were surrounded by areas of marked brownish pigmentation. The external genitals were those of a normal uncircumcised male child.

The abdominal wall was extremely thin and free from fat. The peritoneum was smooth and glistening. The abdominal cavity was free from fluid, pus, and adhesions. Omental fat was very scanty. The lower border of the liver lay 5 cm. below the right costal margin. The height of the diaphragm was at the fifth intercostal space on either side. The mesenteric glands were normal in size, color, and consistency. The pleura of either side was smooth and glistening. Both pleural cavities were free from fluid, adhesions, and pus. The pericardium was healthy. The cavity contained about 3 c.c. of clear, straw-colored fluid.

The thymus was very small, weighing 3 gm., and was normal in position and structure. The thyroid showed no gross pathologic change. The heart was smaller than usual and occupied a more perpendicular position. It extended 3.5 cm. to the left of the midline in the fourth intercostal space. It weighed only 77 gm. (approximately one-half the average weight for his age) and measured 7 cm. in length by 5.5 cm. in width. All chambers were in a moderate degree of dilatation. They contained dark red, fluid blood. The valves all appeared healthy. The circumference of the respective valves was as follows: tricuspid 7 cm., pulmonary 4 cm., mitral 6 cm., aortic 4 cm. The right ventricle wall measured 3 mm. in thickness, the left ventricle wall 6 mm. The myocardium was of a good red color, but it was rather flabby. The aorta just distal to the origin of the great vessels measured 3 cm. in circumference. The foramen ovale and ductus arteriosus were closed. There were no abnormalities of the great vessels. There was an early terminal lobular pneumonia in the posterior part of the right lower lobe. The liver weighed 673 gm. It was of a dark, reddish brown color and appeared normal. The spleen weighed 72 gm. The surface was smooth, dark red, and of normal consistency. On section, the malpighian corpuscles were distinct. There was a slight excess of splenic pulp. The right kidney weighed 56 gm., the left 64 gm. Neither showed any pathologic change. The urinary bladder contained about 50 c.c. of clear amber-colored urine. The pancreas appeared healthy. The gastrointestinal tract showed nothing worthy of note. Permission to examine the head was refused.

The *suprarenals* were very small. The right weighed 1.4 gm., the left 1.6 gm., the average normal weight being 7 gm. They were normal in position but could be distinguished only with difficulty from the surrounding fat, which was scanty in amount. The surface was of a dark brownish red color. Cross-section of the left suprarenal revealed a very thin gland, except the region toward one end, which was bulbous. The thin portion measured scarcely more than 1 mm. in thickness, while the bulbous portion measured 4 mm. at its thickest point. The thin portion appeared tough and of a pale pink color, while the entire thickness of the bulbous portion, with the exception of the capsule, was composed of a brownish red mass resembling medulla rather than cortex. Nothing of the nature of cortex could be identified with the naked eye. The right gland was still smaller, and except for two small nodules, one near the middle of the cross-section and another at the end, the gross appearance was similar to that of the thin portion of the left gland, its average thickness being not more than 1 mm. These two small nodules were also of a brownish red color, and they extended from the capsule on one side to the capsule on the other side. One measured 3 by 4 mm. and the other 3 by 2 mm. in their greatest dimensions.

Report of Microscopic Findings.—The microscopic appearance of the two suprarenals was quite similar with the exception that, while some cortical cells remained in the left gland, none whatever could be found in the right. In the left gland the capsule was slightly thickened, and throughout the greater part of the thin portion

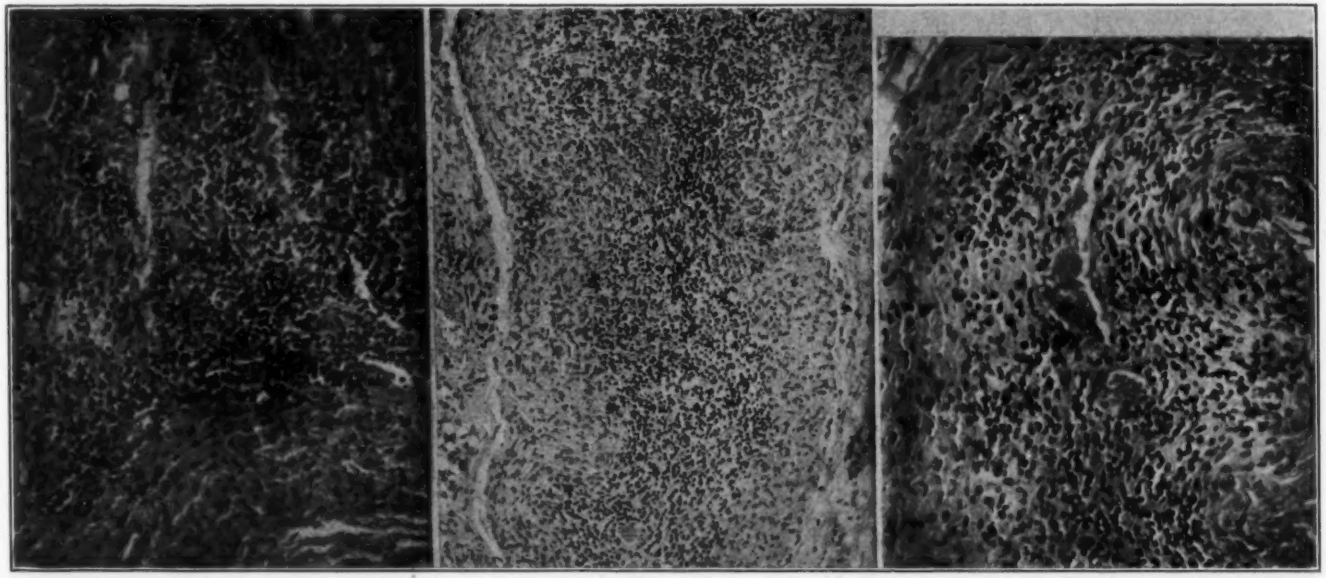

Fig. 3. Fig. 4. Fig. 5.

Fig. 3.—Left suprarenal. In part of the field may be seen a portion of the capsule; elsewhere the remains of a few cortical cells, widely separated by numerous small round cells. Hematoxylin and eosin, ×200.

Fig. 4.—Right suprarenal. The capsule of one side is separated from that of the opposite side by a vascular "core" thickly infiltrated with small round cells but at this point showing neither cortical nor medullary cells. Hematoxylin and eosin. ×120.

Fig. 5.—Right suprarenal. Higher magnification of another field showing the vascular "core" with capsule on either side. Hematoxylin and eosin, ×200.

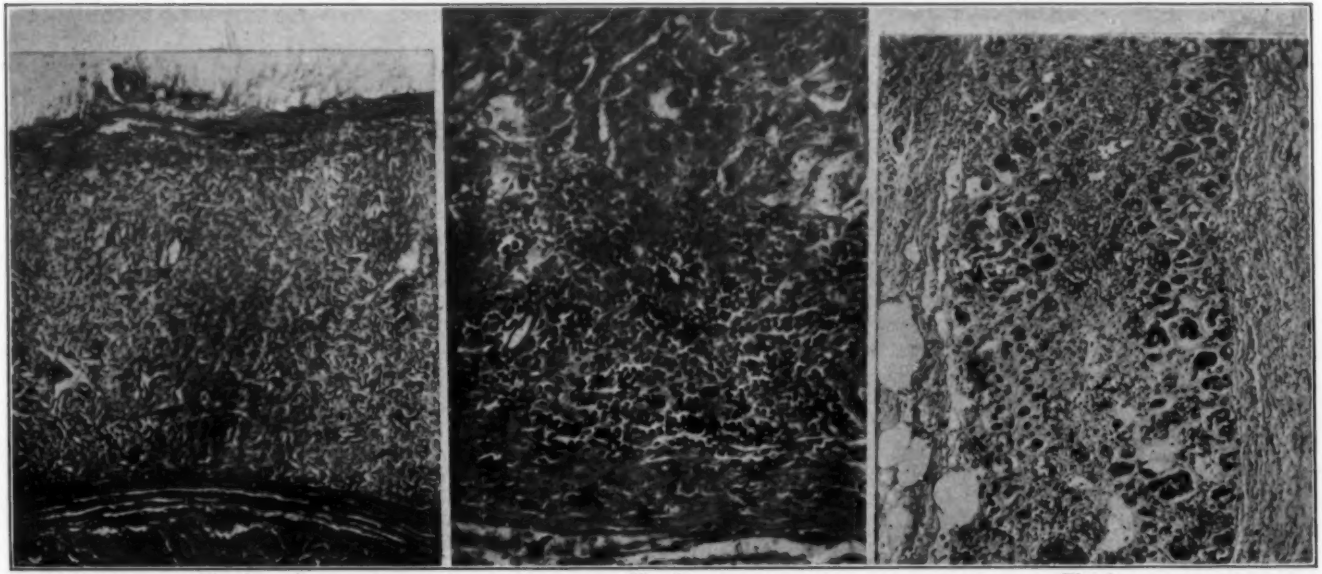

Fig. 6. Fig. 7. Fig. 8.

Fig. 6.—Left suprarenal. Section through the "bulbous" portion of the gland. Here no cortex whatever is visible between the medulla and the capsule. Hematoxylin and eosin, ×60.

Fig. 7.—Left suprarenal. Small zone of atrophied cortex between capsule and medulla. Hematoxylin and eosin. ×200.

Fig. 8.—Atrophy of suprarenal in a boy, ten years old, who died of tetanus, eighteen months after severe attack of diphtheria. Hematoxylin and eosin. ×120.

of the gland the capsule of one side was separated from that of the opposite side by a thin layer of vascular connective tissue which was thickly infiltrated with small round, rather deeply staining cells (Figs. 3, 4, and 5). The degree of infiltration varied greatly from field to field. In this adrenal "core" one could recognize a few small clumps of cortical cells and at one point a few sympathetic ganglion cells such as are occasionally seen in the normal medulla. No chromaffin cells were found in this portion of the gland. The picture in the bulbous part of the gland, however, was quite different. Here the whole of the space bounded by the capsule on either side was filled with chromaffin cells, which so far as one could tell, were normal (Fig. 6). Here no cortical cells whatever were to be seen, but immediately underneath the capsule there was a narrow zone of round-celled infiltration. In the region in which the bulbous portion shaded off into the thin portion, there was an irregular conglomeration of cortical cells, small round cells, and thin-walled blood vessels (Fig. 7). Nowhere did the arrangement of cortical cells bear any resemblance to the normal structure, so that one was unable to determine to which particular cortical zone these cells had originally belonged. Some of them were smaller than normal, and in some the nuclei stained poorly. No groups of cells which were interpreted as islands of regeneration were seen, and no pathologic changes were observed in the blood vessel walls.

Microscopic examination of the other organs including the thymus and testicle revealed nothing worthy of note except one small area in the thyroid in which there was some atrophy of a small group of gland acini with fibrosis and interstitial lymphocytic infiltration.

DISCUSSION

Addison's disease was originally described as resulting from tuberculosis of the suprarenal gland. Atrophy of the gland with no evidence of tuberculosis has been recognized by many as the cause of clinical manifestations which are indistinguishable from Addison's disease.

The patient with Addison's disease presents the following symptoms and signs: weakness, lassitude, gastrointestinal disturbances with vomiting and diarrhea, pigmentation of the skin, susceptibility to infection, poor reaction to injuries, low blood pressure, and emaciation. Anorexia, especially for fats, is marked. The disease is usually fatal.

Experimentally, suprarenalectomized animals show hemoconcentration, loss of weight, anorexia, low temperature, low basal oxygen consumption, weakness, vomiting, diarrhea, diminished blood flow, low blood pressure, progressive rise in the nonprotein nitrogen level, fall in plasma chlorides and total base.[1] These effects are the result of total extirpation of the gland and may be due in part to loss of medulla, whereas in the human Addison's disease, particularly when due to atrophy, while the cortex is destroyed, the medulla in some instances is comparatively unchanged. The recognition of this atrophy of the cortex in the presence of an intact or almost intact medulla, has led to the belief that the symptoms of Addison's disease are the

result of damage to the suprarenal cortex and not to the medulla. Fig. 6 illustrates the extent to which this cortical atrophy may go in the presence of a normal medulla.

Of the two types of Addison's disease, those cases resulting from tuberculosis are more numerous than those in which atrophy is the outstanding lesion. Guttman[2] in a review of thirty-three cases gives the relative proportions in the two groups as 1 of atrophy to 3.5 of tuberculosis. Similar figures are reported by Heller,[3] who in a series of 12,000 postmortem examinations had twelve cases with clinical symptoms of Addison's disease. Six of these were due to tuberculosis and three to atrophy. In addition to these nine cases, he encountered in the same series eighteen other cases of tuberculosis of the suprarenal and five cases of suprarenal atrophy in which the clinical symptoms of Addison's disease were lacking.

While Addison's disease may occur at almost any age period with the exception of infants and very young children, it reaches its maximum about the forth decade. A few cases of the tuberculous type have been reported in the second half of the first decade, and in the first half of the second decade, while the majority of cases occur between the ages of twenty-five and sixty years. Of the cases reported in the earlier age groups, that is up to fifteen years of age, all have belonged to the tuberculous group. The age of our patient was nine and one-half years. This appears to be the youngest case of suprarenal atrophy reported up to this time.

Guttman[2] pointed out that, if pigmentation appeared early, the course of the disease was prolonged, whereas if pigmentation appeared after the weakness and asthenia were established, death soon followed. The case reported here ran a rapidly progressive course and showed little pigmentation which appeared late in the disease.

The craving of these patients for salt has been previously noted. Ball and Lansbury[4] observed that one of their patients had a craving for salt and olives after the onset of the illness, and they state that this symptom was noticed in two other patients under their observation. This craving for salt was a striking feature in our case, and it is probable that this symptom could be elicited more frequently if inquired for in the history. Marine and Baumann[5] found that suprarenalectomized cats were kept alive for a considerable period on suprarenal extract dissolved in saline. Since they thought that the effect might be due to the saline, the cats were given saline alone or Ringer's solution, and the period of survival was as long as with cortical extract. Following this, attention became centered on sodium. Loeb[6] found a low serum sodium content and an increased potassium level in three cases of Addison's disease. Loeb and his associates[7] in balance studies on suprarenalectomized dogs confirmed the

low serum sodium and raised potassium levels. The chloride and bicarbonate contents of the serum were decreased. The excretion of potassium was normal, but the sodium and chloride contents in the urine were increased in total as well as in concentration. The increase in sodium excretion was much higher than the chloride. They concluded that the adrenal cortex probably regulates sodium metabolism. Loeb and his coworkers[8] with balance studies on patients found similar results. If a low salt diet were given, the symptoms were more marked, and immediate improvement followed when 10 gm. of salt were added to the diet. Sears[9] found low sodium and high potassium levels in serum, but after a high sodium chloride diet the sodium and potassium assumed normal levels. Baumann and Kurland[10] found the same in cats, but rabbits had a much less marked change in the sodium and chloride content. Harrop and his associates[1] found a fall in plasma chlorides and total base with a progressive rise in nonprotein nitrogen in experimental animals. There was a negative sodium and chloride balance and increased excretion of urine. These changes were returned to normal with the use of cortical hormone. They concluded that adrenal cortex regulated sodium chloride and water metabolism. Harrop and his associates[11] found in another study that the blood volume and tissue fluids were decreased, that the serum protein was raised, that the urine volume increased, and that there was a negative water balance.

Microcardia, as observed in our patient was also noted by Cushing,[12] who thought it was due to the decrease in blood volume. In his patient when the blood volume was increased by intravenous therapy, the size of the heart increased to normal. This, however, would hardly seem to be the only explanation in our case, since at the postmortem the heart was found to weigh only 77 gm., approximately half the normal weight for a child of that age. Wright-Smith[13] in the postmortem report of his case states that "the heart was very small" but gives no weight. Other organs including thymus, aorta, lungs, liver, kidneys, pancreas, and spleen he also describes as being "small or very small." Hemoconcentration and a low potential in the electrocardiogram were noted by Scott,[14] but no details were recorded as to the size of the heart on physical or roentgenologic examination or at autopsy.

Brenner[15] collected forty-two cases of suprarenal atrophy and added five of his own. In discussing the etiology of the process, he mentioned three possible causes: (a) congenital hypoplasia, (b) chronic inflammation (including tuberculosis, syphilis, and simple inflammation), (c) simple atrophy of the cortex and later of the medulla. While he arrived at no conclusion, he favored the last view and suggested that the process was one of necrosis of cortical cells caused by

some unknown toxin with a special affinity for these cells. He mentioned the possibility that the few cortical cells that remain after the initial injury may be overworked and as a result may undergo a subsequent degeneration or atrophy.

Such a possible etiology is worthy of consideration. As Aschoff[16] pointed out, the suprarenal cortex may show a loss of lipoid in such acute infections as diphtheria and scarlet fever while the medulla remains practically intact. That toxins such as result from these acute infections may be the cause of the initial lesion in certain cases at least seems probable. Proof, however, that this is the case is lacking. Recently there died of tetanus in the Hospital for Sick Children a ten-year-old boy who eighteen months previously had suffered from a very severe attack of pharyngeal diphtheria with toxic myocarditis. He died seven days after the onset of tetanus symptoms. The autopsy revealed a marked difference in size of the two suprarenals, the right weighing 5 gm. and the left 9 gm. Microscopically the right suprarenal showed areas of atrophy of both cortex and medulla with slight round-celled infiltration as shown in Fig. 8. Whether or not this was in any way the result of the action of the diphtheria toxin eighteen months previously cannot be said. The lesion appears to be of longer standing than the duration of tetanus symptoms. In the case of Addison's disease reported here, there was on the other hand no history of either diphtheria or scarlet fever.

Wahl[17] interpreted small round cells in his case of atrophy as embryonic neurocytes and pointed out that they bore a certain resemblance to the small round cells seen in malignant tumors of the adrenal medulla—the neuroblastomata. He supported the view of Bloch,[18] who advanced the theory that the condition is not one of true atrophy, but is rather the result of a perversion of the normal process of development of the suprarenal medulla during fetal life. Normally the embryonic neurocytes which migrate through the cortex, eventually form the medulla, but with the increase in size of the medulla there is a corresponding atrophy of the inner zone of the cortex with a simultaneous regeneration of the glomerular zone. According to Bloch, if this process of atrophy of the inner zone of the cortex is perverted and prolonged into early childhood or later life, the great bulk of the cortex may eventually disappear, having been replaced by embryonic neurocytes. While this theory is very interesting, it appears to have received little acceptance.

In some of the so-called atrophy cases no suprarenal tissue at all could be found.[35] These patients probably originally had suprarenal tissue which later disappeared because absence of the suprarenal at birth is usually associated with anencephaly. This absence, however, is not constant. In two cases of anencephaly recently studied by us,

in one in which death occurred within twenty-four hours of birth no suprarenal tissue whatever could be found, while in the other case in which death occurred on the second day, small but well-formed suprarenals were found above either kidney. These showed both cortical and medullary tissue.

Regeneration of cortical cells in glands showing also marked atrophy has been reported,[26, 27] but no nodules which might be interpreted as such were seen in our case.

Changes in other ductless glands, such as the thyroid and the pituitary, have been reported.[3, 15, 19, 20, 21] In some instances these glands show an atrophy and infiltration with small round cells. Nothing of this nature was found in our case except for a small focus in the thyroid gland, which may not be related to the adrenal lesions. Unfortunately, since permission to examine the head was refused, we have no knowledge as to the condition of the pituitary gland.

In the treatment of this condition many forms of therapy have been tried, and only recently has success of any degree rewarded the efforts. The Muirhead treatment[22] was used which consisted of giving adrenalin hypodermically and by rectum and whole gland by mouth. The results were disappointing. Ibotson[23] records a case treated with anterior pituitary gland, bovril, soda, and milk by mouth. He attributes the improvement to the pituitary gland therapy, but in the light of recent work it may have been the soda. Marsh[24] reports two patients treated with suprarenal extract by mouth, one of whom lived twenty-one years. Rogoff[25] experimentally and later with Stewart[26] clinically found that there was improvement following the injection of an extract they called interrenalin along with Ringer's solution.

Rowntree and his associates[28] report twenty cases treated with cortical extract of Swingle and Pfiffner. The majority of patients did well. The high cost of the material and the large amount of suprarenal tissue necessary to produce it made it prohibitive for general use. Ball and Lansbury[4] made a similar report but Scott[14] found no improvement using this extract.

Harrop and his coworkers[1, 11, 29, 30] found that suprarenalectomized dogs lived normally on cortical extract. They also found that with patients suffering from Addison's disease, the hypotonia, asthenia, low blood pressure, sensitivity to thyroid and insulin, and malnutrition continued in spite of the administration of the extract. Hartman, Aaron and Culp[31] report an amelioration of symptoms in a patient by the use of cortin, but there was a relapse as soon as treatment was stopped.

As mentioned before, Marine and Baumann[5] found in 1927 that the life of suprarenalectomized cats could be prolonged as well with the use of sodium chloride solution as with cortical extract. Since then

sodium chloride has been used with patients and in experimental animals. Harrop and his associates[29] treated patients with a high salt diet and, if there was a relapse, used the cortical extract that was potent for dogs. Loeb and his coworkers[6, 8, 32] reported their observations in experimental animals and humans of the use of a high salt diet and found that 10 gm. of salt added to the diet daily relieved the symptoms almost immediately in a large proportion of cases. These patients have lived over considerable periods. Similar results are reported by others.[9, 10, 12, 33] There is a report of one case[34] with complete recovery in which no specific treatment was given. The author diagnosed it as a suprarenalopathy.

SUMMARY

Several features are of interest in the case reported. The age was nine and one-half years, which is probably the youngest on record. The craving for salt observed by the parents was significant. The microcardia was noted by Cushing[12] about the same time as we observed it in this case. The temporary improvement with adrenalin and continuous intravenous therapy was probably due to the saline. Marked asthenia, emaciation and weakness preceded the low grade pigmentation, and the course was rapidly fatal. The improvement following the administration of salt was striking but not sustained. The blood sugar curve was prolonged, somewhat diabetic in type. The electrocardiogram showed a low potential. The child died following a series of convulsions which may have been a manifestation of hypoglycemia. The cause of the atrophy remains obscure.

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Critical Review

ENDOSCOPY

A Review of the Recent Literature With Comments

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THERE is a notable increase each year in the number of publications on the subject of endoscopy as related to diseases of childhood. The term "endoscopy" as herein employed includes direct laryngoscopy, bronchoscopy, and esophagoscopy.

Bronchoscopy formerly was thought of mainly as a means of removing a foreign body in the lung or esophagus, whereas today, according to Chevalier Jackson,[1] only about 2 per cent of the cases are so handled for this reason, the remaining 98 per cent being studied for disease of the respiratory tract of one kind or another. Jackson also advises early bronchoscopy in postoperative cases with lung complications in which bronchial obstruction by blood clot or thick mucus is suspected. He refers to the fact that "The internist stops, looks and listens, the x-ray man looks through, while the bronchoscopist actually looks inside the patient." The necessity of teamwork on the part of the pediatrician or general practitioner, roentgenologist and bronchoscopist must be emphasized. Since the general practitioner is the one who is usually first to see patients after foreign body accidents or with pulmonary affections, his part in the management of such cases will probably have a direct influence on the patients' future courses. It is especially important for him to keep in mind that immediately after the aspiration of a foreign body, there is likely to be what is termed a symptom-free period, when the patient may have few or no symptoms. However, if such a patient be carefully examined, both physically and roentgenologically, definite signs of bronchial or tracheal obstruction will usually be found if a foreign body is present.

It is necessary for the general practitioner to make a differential diagnosis between such conditions as the presence of foreign body, tuberculosis, pneumonia, lung abscess, bronchiectasis, and other pulmonary affections. The importance of correct differential diagnosis is better appreciated when we realize that in the presence of foreign body, prompt bronchoscopy is indicated whereas in some of the other conditions enumerated it may or may not be indicated.

Certain special signs which indicate the presence of foreign body in the air passages have been described by Chevalier Jackson, among which is the "asthmatoid wheeze." This is heard best by placing the bowl of the stethoscope or the ear before the open mouth of the patient. Parents will often describe the development of such a wheeze after an accident, but sometimes it must be brought out by question-

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ing. The "audible slap" caused by impact of the foreign body against the under surface of the vocal cord on coughing is also heard in front of the open mouth or with the stethoscope placed over the larynx. The same impulse, when obtained by placing the palpating fingers over the larynx, is called the "palpatory thud."

The x-ray diagnosis of nonopaque foreign body in the trachea or bronchial tubes, which has been described by Iglauer,[2] Manges,[3] Jackson,[4] Moore, Wilson and Arbuckle,[5] and others, depends upon the partial or total obstruction of a given section of the bronchus or trachea by the foreign body with consequent changes in the air content of the entire pulmonary tract and with characteristic displacement of the thoracic viscera and the diaphragm. Such a case (Case 1, Plates 1 and 2[6]), with a diagnosis of suspected foreign body in the lung based on the physical findings, was seen by us and confirmed by x-ray examination and bronchoscopy. The history is of extreme importance and often is discounted to the patient's disadvantage because of the fact that the patient is then within the symptom-free period. In this

Plate 1. Plate 2.

Plate 1.—Case 1. Made at the end of full inhalation, and showing the apex of the heart almost in normal position while the base of the heart and the aorta are markedly displaced to the right.

Plate 2.—Case 1. The apex of the heart is displaced to the right as is also its upper portion. This is the result of inflation and deflation of the right lung with atelectasis of the left lower lobe and obstructive emphysema of the left upper lobe. The diagnosis of nonopaque foreign body in the left bronchus with atelectasis of the left lower lobe and obstructive emphysema of the left upper lobe was made by Dr. Hugh Wilson in the absence of history of foreign body accident and before bronchoscopy. It was confirmed at bronchoscopy. The foreign body was a fragment of mulberry switch which had been placed within the infant's reach by an older child.

case, however, there was no history suggesting aspiration of a foreign body, but the physical findings could not be explained on any basis other than that of foreign body aspiration (Plates 1 and 2).

Chevalier Jackson also calls attention to the very low mortality rate in foreign body cases when the bronchoscopist is properly trained and equipped and when the use of a general anesthetic is avoided. In addition, he refers to the practice of direct laryngoscopy in infants and children as a means of establishing a correct diagnosis. With one quick look the condition of the larynx can usually be determined, and only by this means can it be seen.

J. D. Kernan and A. J. Cracovaner[7] comment on the increasing popularity of endoscopy among medical men who have had actual

experience with this method of diagnosing disease of the larynx, tracheobronchial tree, and esophagus.

V. E. Negus[8] speculates on certain features of the mechanics of respiration as an etiologic factor in lung disease and also says the value of bronchoscopy in diagnosis and treatment cannot be overestimated.

The diagnosis of laryngeal disorders in infants and young children, such as the congenital abnormalities, deformities seen in rickets, papilloma, impacted foreign body,[9] streptococcic infection, diphtheria, syphilitic disease, or disorders immediately below the larynx simulating laryngeal disease, usually can be made out by this method of study. In the case of a three-and-one-half-year-old girl (Case 2), recently seen by the writer,[10] signs and symptoms pointed to laryngotracheal obstruction (Plates 3, 4, and 5). Direct laryngoscopy was negative, but marked compression of the trachea with a high degree of obstruction was readily visible through the bronchoscope. This was caused by a tumor, which was demonstrable in the plates and which has entirely disappeared, as have all symptoms after deep therapy.

John H. Foster[11] reports very interesting experiences with the treatment of papilloma of the larynx in children by radiation therapy. He prefers to have these patients irradiated without operation if possible, but he has irradiated some in whom it was necessary to operate for laryngeal obstruction. The necessary observations in these cases must be carried out by direct laryngoscopy.

Moore, Wilson, and Arbuckle[5] described the x-ray appearance and symptoms produced by foreign body in the trachea and ascribed as a cause of sudden death, in some of these cases, interference with the return blood supply to the heart instead of asphyxiation due to tracheal obstruction. This interference with the circulation is the result of compression of the mediastinum and its contents on both sides by a marked bilateral obstructive emphysema when the foreign body is in the trachea. The cardiac shadow assumes a typical shape and the diaphragm a typical position (Case 3, Plates 6, 7, and 8[12]). The foreign body in this case shifted back and forth between the trachea and one or the other bronchi with constant coughing. Wilson was able to demonstrate bilateral obstructive emphysema when the foreign body was in the trachea and unilateral obstructive emphysema when it was in either right or left bronchus.

W. D. Stovall and H. P. Greeley[13] describe the bronchoscopic findings and treatment in bronchial mycosis with very satisfactory results.

C. A. Heatly[14] points out the use of bronchoscopy as a valuable adjunct in the diagnosis and treatment of bronchopulmonary suppuration and emphasizes the importance of collaboration between the bronchoscopist, internist or pediatrician, roentgenologist and thoracic surgeon.

W. F. Moore[15] remarks on the value of bronchoscopy in all types of lung suppuration and points out that it is a safe procedure in children when carried out by a qualified bronchoscopist.

W. B. Faulkner,[16] in referring to postoperative complications, gives a striking example of the value of bronchoscopic examination for cases of bronchial obstruction and the necessary treatment.

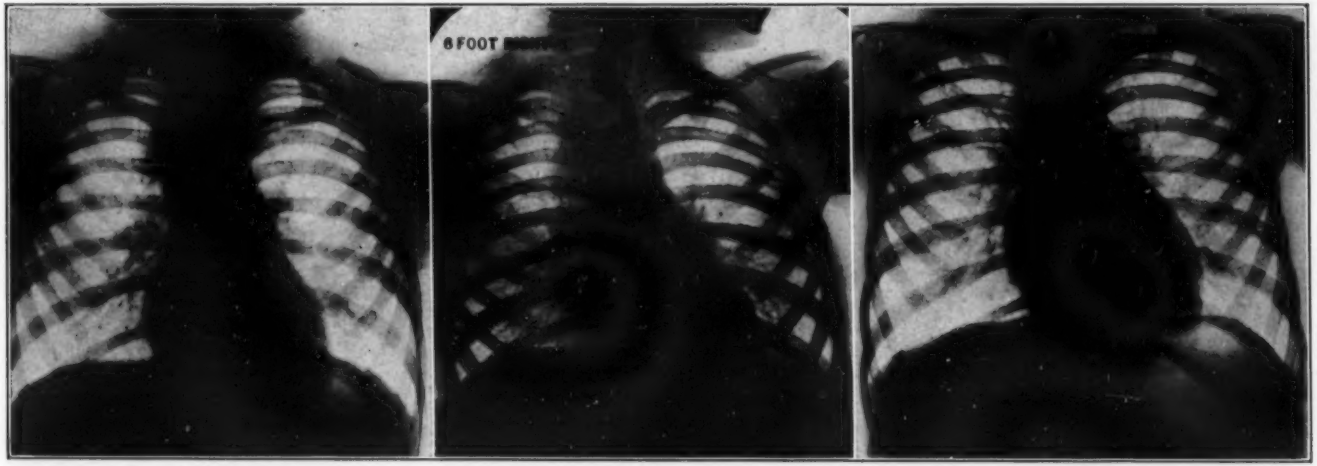

Plate 3. Plate 4. Plate 5.

Plate 3.—Case 2. June 8, 1935. Showing a mass to the right of the trachea and esophagus high up in the chest.

Plate 4.—Case 2. June 10, 1935. Showing deviation of esophagus with barium.

Plate 5.—Case 2. July 23, 1935. Showing almost total disappearance of the tumor. At this time the child had no subjective or objective symptoms, and bronchosocopy was deemed unnecessary.

A. J. S. Pinchin and H. V. Morlock[17] discuss the diagnosis and treatment of lung abscess and bronchiectasis by bronchoscopic methods, with a comparative report of cases so treated as a means of curing a large percentage of abscesses and as a palliative measure in bronchiectasis.

Graham and Singer[18] have shown the importance of classifying cases of bronchiectasis and of localizing the area of involvement. These authors and many others stress the importance of at least one bronchoscopic examination in all such cases in order to rule out suspected foreign body and also as an aid in localizing the diseased area. They and others have been able to report very encouraging results after surgical interference in properly selected cases.

The late E. H. Funk[19] discussed the great value of bronchoscopy in the study and treatment of chest diseases, such as abscess, bronchiectasis, and carcinoma. He laid emphasis on the importance of cooperation between the internist, roentgenologist, bronchoscopist, and thoracic surgeon "if we are to attain the maximum of diagnostic accuracy and therapeutic success." In urging bronchoscopic study, and in answer to those who decry its value, he referred to the controversy which arose at the time when the stethoscope was first introduced and concludes that new methods, when worth while, merely emphasize the value of those already established.

W. A. Hudson[20] calls attention to the ever increasing value of bronchoscopy in thoracic disease as its usefulness becomes more generally appreciated.

Many articles have been written on the value of bronchography by the introduction of radiopaque substances through the bronchoscope as a diagnostic as well as therapeutic method. R. B. W. Ellis[21] describes his method of injecting lipiodol by means of a needle introduced through the cricoid thyroid membrane. Barring accidents, such as have been reported with this method of introduction, we still are deprived of information obtained by direct examination of the tracheobronchial tree, such as the possible presence of a congenital stricture, tumor, foreign body, etc., which are recognized causes of lung suppuration.

An interesting preliminary report of a new method of physical study of the lungs, individually, with particular regard to vital capacity, is reported by H. C. Jacobaeus and his associates.[22]

Clerf[23] thinks highly of bronchoscopy in the treatment of bronchiectasis in children.

John Alexander and W. E. Buckingham[24] say, "In all cases of bronchiectasis there is a special indication to treat an infected mouth and sinuses and to search with the bronchoscope for an intrabronchial foreign body that may not be visible roentgenologically." They also say, "Obstruction of the bronchus by cancer or benign tumor should be ruled out, as should an empyema with bronchopleural fistula."

In obstructive disease of the esophagus, both acquired and congenital, inspection and treatment with the aid of esophagoscopy have done much toward solving the difficult problems herein encountered, as well as in reducing the mortality rate. Gabriel Tucker[25] a few

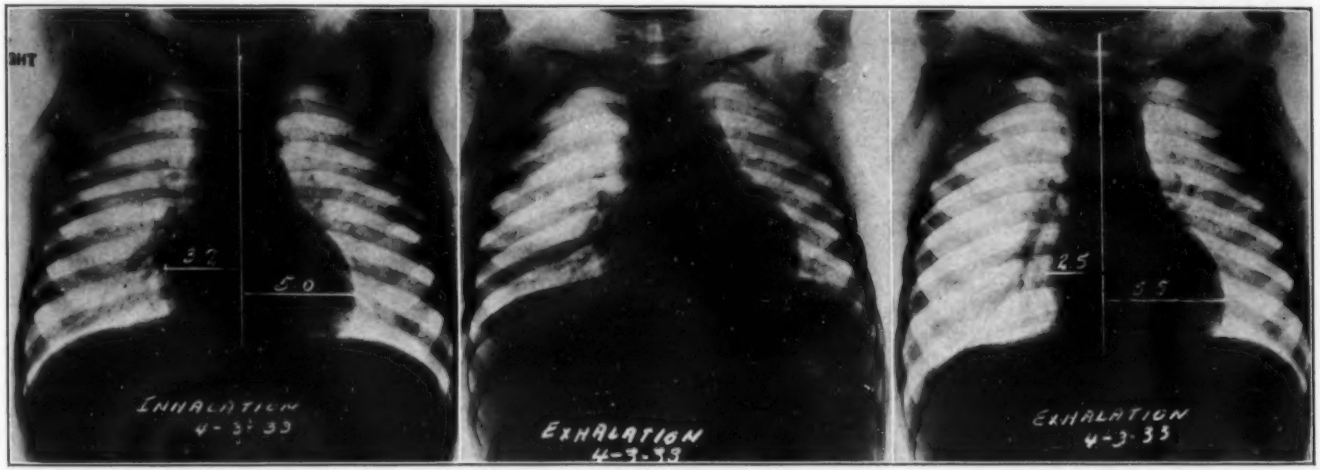

Plate 6. Plate 7. Plate 8.

Plate 6.—Case 3. Made at the end of full inhalation showing marked bilateral emphysema, with the heart and diaphragm practically in normal position.

Plate 7.—Case 3. Made at the end of full exhalation showing obstructive emphysema of the right lung with some displacement of the heart to the opposite side and with a somewhat flattened dome of the diaphragm. The physical signs of emphysema, such as suppression of breath sounds and a raised percussion note over the right lung, where demonstrated.

Plate 8.—Case 3. Within a few moments after an attack of coughing, the same physical signs were present in both sides of the chest and an x-ray plate made at this time demonstrated a much narrowed heart shadow with increased emphysema on both sides and flattened dome of the diaphragm on both sides. It is evident that there was marked compression of the mediastinum and heart from both sides.

years ago described retrograde bouginage for stenosis of the esophagus, thereby conferring a great boon on the patient as well as the physician.

The age of incidence and the length of time a foreign body has remained in the lower air or food passages of an infant is at times surprising. For example a child, aged three and one-half years (Case 4[26]), was brought in with a safety pin in his esophagus; there was a definite history of its having been present since the age of six months (Plate 9). This was successfully removed endoscopically. Murdock Equen[27] has written on the treatment of foreign body imbedded in the wall of the esophagus and removed by dissection through the esophagoscope. He points out the necessity of maintaining the patient's state of nutrition by gastrostomy, if need be, in the presence of obstruction of the esophagus.

All esophagoscopists realize that water hunger constitutes a definite contraindication for esophagoscopy until this want has been supplied

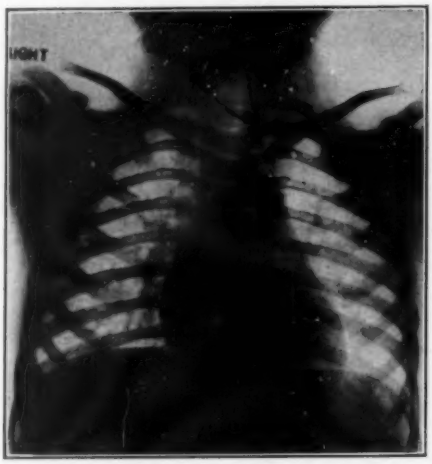

Plate 9.—Case 4. Demonstrating safety pin in the esophagus, which had perforated the wall of the esophagus and was surrounded by granulation tissue because of the long-continued irritation. Apparently there was a considerable abscess immediately outside the wall of the esophagus since after the pin had been disengaged there was drainage of pus into the lumen of the esophagus.

because the degree of shock under such conditions is out of all proportion to the manipulation necessary.

E. J. Patterson[28] and Jackson and others have reported removal of a benign tumor from the esophagus. Patterson[29] also reports an interesting case of foreign body in an infant two months old.

T. R. Gittens[30] discusses diagnosis and treatment of nondiphtheritic inflammatory disease of the larynx and trachea in infants and young children.

M. P. Stiles[31] reports his observations of a series of cases of vegetable foreign bodies in the trachea and bronchi.

A. Soulas[32] stresses the value of systematic bronchoscopic study and treatment and reports gratifying results in a rather large series of cases of pulmonary suppuration.

V. Cordier and P. Mounier-Kuhn[33] comment on the value of bronchoscopic treatment of lung suppuration with a fairly large percentage of good results from a palliative standpoint and cure in a small percentage of cases.

Bronchoscopists and pediatricians should bear in mind the fact that whereas in children, especially young children, the utmost care is necessary in carrying out endoscopic procedures, it is also true that response to treatment is comparatively better and the percentage of curability greater, particularly in cases of chronic lung suppuration. This probably is due to the fact that the disease in children has not had time to become so widely distributed throughout the pulmonary tract or so deeply invasive as is so often true in adults.

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539 North Grand Boulevard

American Academy of Pediatrics

Proceedings

FIFTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

NEW YORK CITY, JUNE 7, 1935

Round Table Discussion on Whooping Cough

The meeting was called to order by Dr. William H. Park, of New York City.

CHAIRMAN PARK.—I shall open the discussion of "Pertussis Prophylactic Vaccination," which will then be continued by Dr. J. M. Frawley of Fresno, Calif., who will discuss whooping cough treatment and Dr. L. W. Sauer of Evanston, Ill., who will discuss whooping cough; immunization with vaccine—a seven-year report.

There is at present considerable difference of opinion as to the dosage of pertussis vaccine to be used for immunization. Dr. Sauer has doubled and quadrupled the doses that most us were using when he began his work, while Dr. Madsen, of Copenhagen, has recommended a smaller dosage.

Dr. Sauer recommends the use of freshly isolated strains which have been grown on media containing human blood. We, on the other hand, feel that stock strains which are kept under optimum conditions in the laboratory and are grown on sheep's blood will be equally antigenic. It seemed desirable, therefore, that we discuss and determine, if possible, the following points:

1. The optimum dosage to be used.
2. The comparative value of intramuscular and intracutaneous vaccination.
3. The antigenicity of newly isolated cultures (Sauer vaccine) and of suitable stock strains (Mishulow vaccine).
4. Optimum intervals between injections, i.e., two days or one week.
5. The agglutinin response after vaccination. We feel that considerable information may be obtained from the antibacterial antibody response as to the antigenicity of a vaccine, although we realize that these humoral antibodies disappear in time and yet the children may remain immune.

The Pertussis Vaccines Employed in This Investigation Were as Follows.—1. *New York City Department of Health (Mishulow):* Stock cultures are used that are typical morphologically, culturally, and serologically.

These cultures are grown on sheep's blood agar to which 1 per cent of sheep's serum broth is added after inoculation. Vaccines grown in this manner contain, in addition to the pertussis bacilli, a toxic substance which increases the stimulation of agglutinins.[1]

2. *Sauer Vaccine:* Freshly isolated strains of pertussis are grown on human blood, Bordet-Gengou medium and the growth suspended in 0.5 per cent phenol in saline, and the vaccine is refrigerated for one week. After it is found sterile, the vaccine is further diluted with 0.5 per cent phenol in saline to contain 10 billion bacteria per cubic centimeter.[2]

Our clinical tests were carried out at two institutions: (1) The New York Foundling Hospital under Dr. T. E. Waldie. This is a large Catholic children's institution where some of the children are born, and others are brought in and then are boarded out to families who return them to the hospital if they develop any infection such as whooping cough, measles, etc.; and (2) at the Hamilton Center, Henry Street Visiting Nurses Association, under Dr. W. Y. Shorr. This is a small nursery for children from two to six years old, which is situated in a very congested section of the city, where there are many cases of whooping cough. The agglutination studies were carried out at the Research Laboratories of the New York City Department of Health by Miss Mishulow and her assistants.

The children in the above institutions were divided into groups and were given varying doses of the vaccine by the intramuscular, by the intracutaneous, and by the subcutaneous routes (only a few by the last method). Some of them were injected with the vaccine at two-day and others at seven-day intervals. A fairly large group of children was injected with sterile milk instead of vaccine; these served as controls; also a large group of unvaccinated children was kept under observation under the same conditions as the vaccinated children.

Of the 559 who received the New York City Department of Health vaccine, 142 were definitely exposed to active cases of pertussis either in the institution or outside; the results are given in Table I.

TABLE I

TOTAL DOSE VACCINE	NO. CHILDREN	NO. EXPOSED	PERTUSSIS CASES	PER CENT
77 to 88 billions	38	6	0	0
30 to 75 billions	148	16	9 (4 atypical)	6.0
12 to 28 billions	116	78	4	3.4
1 to 10¼ billions	220	13	9 (1 atypical)	4.0

The total number of pertussis cases among the 559 children who received the New York City Department of Health vaccine was 22, or 3.9 per cent. Among these are included 5 children who had no whoop, did not vomit, and in whom the cough lasted only two or three weeks. These cases were so atypical that they would not have been diagnosed as pertussis if the children had not been definitely exposed. No cough plates or blood counts were made in these cases. If only the typical cases are considered the incidence of pertussis in this group would be only a little over 3 per cent (97 per cent protection).

Of the 47 children who received the Sauer vaccine only 3 were definitely exposed, and the results were as follows:

TABLE II

TOTAL DOSE VACCINE	NO. CHILDREN	NO. EXPOSED	PERTUSSIS CASES	PER CENT
40 to 80 billions	45	2 (70 billions)	0	0
20 billions	2	1 (20 billions)	1*	50

*Two and one-half months after vaccination.

Since there were so very few definite exposures in this group, it is difficult to compare the incidence of pertussis with that of the New York City Department of Health Vaccine.

Among the control group of 366 children who were given sterile milk instead of vaccine only 9, or 2.5 per cent, developed pertussis. Among the 4,377 unvaccinated controls 220, or 5.2 per cent, developed pertussis.

In addition to the clinical study of the optimum dosage, method of vaccination, and the antigenic value of vaccine prepared by the Sauer and the Mishulow methods, we studied the agglutinin response in several groups of vaccinated children, as well as in corresponding controls. The best agglutinin response was obtained in the children who received the higher dosage of the vaccines, and the average agglutinin response in a group of children who received the Mishulow vaccine was higher than in a corresponding group that received the same dosage of Dr. Sauer's vaccine.* This may have been due to the additional stimulation of the toxic substance that is present in our vaccine.

Conclusions.—From the results obtained in our tests the following conclusions may be drawn:

1. The efficacy of pertussis prophylactic vaccination appears to depend primarily upon sufficient dosage. It seems that in cases in which sufficient dosage was used both vaccines were equally efficacious.

2. The study of agglutinin response also shows that the greatest response was obtained in the group which received the higher dosage and was at its maximum two to three weeks after vaccination.

The results obtained indicate that a total dosage of 50 to 80 billions should be used for prophylactic immunization. Also that intracutaneous vaccination with 30 to 40 billion bacteria may be as efficacious as much larger doses given intramuscularly.

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DR. FRAWLEY.—We have been working for the last few years with undenatured bacterial antigen prepared according to the method of Dr. Krueger. Dr. Krueger directed attention to the rôle which denaturation plays in the destruction of antigens and to the antigenic value of vaccines. He prepares his vaccine without subjecting the organisms to heat or to chemicals in the course of this preparation and believes the quality of the original living bacterial cell is preserved for this reason.

In making a vaccine the logical starting point is to take the organisms first and to utilize the bacterial complexes. There are other elements in the culture which have antigenic value as well, such as the toxic filtrate, which gives the reaction of Schwartzman and which has been shown by Gross and others to be of antigenic value. While that fraction has been sacrificed in this vaccine in order to obtain one that would be nonirritating, there is considerable evidence to show that a sufficient amount, and probably the majority, of the antigenic properties are preserved.

I have used this vaccine both in prophylaxis and in treatment, but only within the last six months have I used it in large doses. The earlier work has been reported.

In January or February a group of 132 kindergarten children were given 12 c.c. of the vaccine subcutaneously, 4 c.c. each week for three weeks; three children from that group have contracted whooping cough. Two of the cases were very mild, and the other one was of moderate severity—however, that child had started a cough at the time he received his last injection. The fact that six other children who were exposed since then have not contracted whooping cough is an evidence of the value of the vaccine in modifying if not absolutely preventing whooping cough.

*Details of this study will be published elsewhere.

Since January I have been giving injections in treatment twice a day using 5 c.c. at each dose; twenty-eight children received this dosage. Table I gives a brief summary of these cases.

TABLE I

PERTUSSIS TREATMENT WITH THE KRUEGER ENDOANTIGEN
(DR. J. M. FRAWLEY) 28 CASES

CASES TREATED	TREATMENT BEGAN	DURATION OF TREATMENT IN DAYS	TOTAL DOSAGE IN C.C.	RESULT
1	Before symptoms	8	60	Atypical, very mild
1	Before symptoms	15	85	Mild
6	2 to 3 days after infection	5 to 7	20 to 60	5 mild, 1 moderately severe
5	5 to 8 days after infection	7 to 12	33 to 53	Mild
1	8 days after infection	17	122	Severe
10	10 to 14 days after infection	5 to 14	25 to 78	3 mild, 7 severe
4	18 to 21 days after infection	5 to 10	25 to 80	Severe

In two instances the children responded to treatment but contracted colds twelve to fourteen days later and had relapses. In one case treatment was begun twenty-three days after infection. The child was whooping and vomiting twenty-four times a day. He received two daily injections of 5 c.c. without any improvement. No injection was made for twenty-four hours; then he was given thirteen injections of 5 c.c. at four-hour intervals and showed marked improvement after forty-eight hours of this intense treatment.

The results in those cases have been very satisfactory. The best results were obtained when the vaccine was used immediately after exposure. Ten children who received their injections at the beginning of their coughing or before they had started to whoop continued to cough after vaccination had begun for an average of eight days. Eighteen children who were first seen in the paroxysmal stage had an average duration of coughing of 9.4 days after starting vaccination. There is not much difference between those two groups, and I found it didn't make much difference at what stage of the disease the injections were begun when such large doses were given.

Four patients did not respond well to vaccine and continued to whoop and vomit regardless of how much vaccine was given. The average duration of the coughing after vaccination was begun in those children was 16 days, and the average duration in the other twenty-four was 7.7 days. The children who were resistant to the vaccine were children who had an upper respiratory infection, such as a nasal discharge, which simulated a common cold. One child during the infection had been definitely exposed to a cold, and the coughing was prolonged. There was no history of exposure to a cold in the other children; nevertheless, they had the symptoms of cold except that it seemed to be more prolonged than the average common cold would be. Whether or not those children were allergic it would be impossible to say. But certainly children who are of the hyperallergic group tend to have a more severe pertussis.

CHAIRMAN PARK.—I hope that after Dr. Sauer has finished that this question of filtrable virus may be taken up by some of the members.

DR. SAUER.—In Table I is summarized the immunization work for the past seven years. Each child was injected with a total of 8 c.c. of potent pertussis vaccine (1 c.c. = 10,000 million *B. pertussis*). Injections had been given at least several months before exposure to infection was presumed to have occurred. The data are based on four sources of evidence:

1. Selected nonimmune children from private practice; in many instances other nonimmune children of the families served as controls. The vaccine was prepared at the Evanston Hospital from recently isolated, hemolytic strains,[1] grown on human blood. In the course of seven years thirty injected children of twenty-four families were intimately exposed to twenty-eight children with pertussis, and all escaped. There occurred, also, 167 casual (outside) exposures, but no injected child contracted the disease.

2. In the Macdonald experiment[2] two of four nonimmune brothers were injected with the vaccine; five months later living bacilli were inoculated intranasally into each of the four boys. The noninjected boys contracted typical whooping cough; the injected boys escaped. The latter failed to contract the disease although intimately exposed to their coughing brothers. This crucial test brings strong evidence of the value of the vaccine as an immunizing agent.

TABLE I

SEVEN-YEAR SUMMARY OF ACTIVE IMMUNIZATION AGAINST PERTUSSIS
(MAY, 1928—JUNE 1, 1935)

8 C.C. TOTAL VACCINE (2, 3, 3 C.C.)	CHILDREN INJECTED	CHILDREN EXPOSED*		FAILURES		PER CENT PROTECTED
Vaccine made at Evanston Hospital (1928-32)	394	F†	30	F	0§	100.0
		O‡	167	O	0	
Macdonald experiment	2		2		0	100.0
Approved commercial vaccine (July, 1932—)	1,002	F	38	F	3	92.1
		O	31	O	3	90.4
Approved commercial vaccine used by 29 physicians in 18 states (1932—)	2,348		76		13	82.9
Total	3,746		344		19	93.0

*Exposure to infection three and one-half months to seven years after injection.
†F, "familial" exposure.
‡O, "Outside" (casual) exposure.
§Three months after injection, a girl aged two years developed mild pertussis from her noninjected (control) brother.

3. One thousand and two nonimmune children (Health Department, 413; orphanage, 159; private patients, 430) were each injected with a total of 8 c.c. of one or the other of two approved commercial vaccines. Three of the thirty-eight injected children who were exposed within the family contracted mild pertussis, and three of the thirty-one injected children, casually exposed, contracted the disease.

4. Twenty-nine physicians in eighteen states injected a total of 2,348 children. Thirteen of the seventy-six children exposed to the disease contracted it, i.e., a failure of 17.1 per cent of the exposed, injected children.

During the past three and a half years a total of approximately 500 homeless "Cradle" infants, less than two months of age, have been injected. The first 425 received 6 c.c.; the remainder, 8 c.c. There have occurred a total of eight exposures, more than four months after the injection; three of the infants escaped; five contracted the disease. As stated, elsewhere,[1] it is questionable whether active immunization of infants so young is possible. It is premature to evaluate this procedure in very young infants.

If properly refrigerated, this vaccine should confer prolonged active immunity in a majority of injected children, provided exposure does not occur within several months after the injection. An immunization schedule in use in private practice by a number of physicians includes pertussis immunization at eight months, diphtheria immunization at twelve months, smallpox vaccination at eighteen months, and scarlet fever immunization at four years. Because whooping cough is more prevalent and serious early in life, pertussis immunization is given first.

Summary.—In a total of 3,746 immunizations of older infants and young children during the last seven years, a total of 344 exposures, with a total of nineteen failures have occurred. Ninety-three per cent of the injected children exposed to infection have not contracted whooping cough.

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DISCUSSION

DR. E. B. FITZ-GERALD (WOLLASTON, MASS.).—I would like to ask Dr. Sauer whether it makes any difference to give the injections at two-week intervals; also would it not be entirely practicable and possible to give children the vaccine at six months?

DR. SAUER.—I have always given it at weekly intervals. Six months is probably all right if the child is exposed within the next three or four months.

CHAIRMAN PARK.—We have tried large numbers of cases at one-, two-, three-, four-, five-, and six-week intervals between doses, and found that two weeks was a little bit better than one week; three weeks was about the same, and after that there was no advantage in extending the interval. I should imagine that two weeks, if you do not mind waiting the time, might give a little better results, but it is probably not of great importance.

DR. T. F. DAVENPORT (ATLANTA, GA.).—From May, 1933, to May, 1935, 300 children were vaccinated in an Atlanta clinic. This report is by Dr. Denmarks who asked me to read it for him. These children had ample opportunity to become infected as there were cases of pertussis in their families. Five of the children developed pertussis—one child, six months and four children, eighteen months after vaccination. Three of these last four children were in the same family. In one case the diagnosis was made by a blood count, cough plate, and by complement fixation. The other four were diagnosed by cough only.

We examined the serums of fifty children for complement fixation. Among these there were some who had vaccine ninety days previously; some who had pertussis previously; some who were whooping, and normal children who had not been vaccinated or exposed to pertussis. In every case in which the child had pertussis or was given the vaccine, the complement fixation result was positive; and in the cases in which the child had neither the vaccine nor pertussis, the test was negative.

DR. LEWIS D. HOPPE (ATLANTA, GA.).—I would like to ask Dr. Park how he gives the intracutaneous vaccine.

CHAIRMAN PARK.—It is given practically like the Schick test. The needle is inserted just under the superficial skin so it can be seen through the skin.

Dr. Waldie, what amount are you giving regularly?

DR. T. E. WALDIE (NEW YORK CITY).—We gave amounts varying from 0.1 to 0.45 c.c. With the 0.45 c.c. we got superficial sloughing in practically every instance. The largest dose we could give without getting a slough was 0.3 c.c. and occasionally it did occur even with that.

DR. FRANKLIN D. WILSON (NORFOLK, VA.).—During the last year we have had an epidemic in the city. I have given the vaccine to approximately 150 children. I do not know how many exposures there have been, but six of those children developed typical clinical pertussis from two weeks to two and a half months after the vaccine. No cases developed after four months so far as I have been able to learn.

I would like to ask Dr. Sauer why it is inadvisable to give other vaccines sooner than four months after pertussis vaccine. Also, aside from the size and character of the colonies, how can the pertussis bacillus be differentiated from the influenza bacillus?

DR. SAUER.—In many cases probably it would not be necessary to wait that long, but it takes about three months to have the immunity complete. Three of our failures occurred in children who had been immunized very soon after they recovered from measles although the whooping cough did not occur until many months later.

A recently isolated pertussis colony and an influenza colony look very different. The pertussis colony is round, spherical, elevated pearly gray, and shiny. The influenza colony is much flatter, seldom spherical, and more translucent. In the smear there is a marked difference. In bipolar staining with the pertussis there is practically no pleomorphism; whereas with the influenza, in any smear, you will see various shapes and types of organisms.

CHAIRMAN PARK.—We perform smallpox vaccinations regularly and a couple of weeks later or a week before diphtheria immunization or scarlet fever immunization. I think it is going to make it more difficult and possibly allow a certain number of children to develop other diseases if we delay the immunization against other diseases.

DR. GEORGE F. MUNNS (WINNETKA, ILL.).—There are several practical points we should consider concerning the administration of pertussis vaccines. One of these is the age at which one should cease to give prophylactic whooping cough vaccine. We do not know how long protection lasts, perhaps for four or five years.

Another point concerns the percentage of protection in pertussis vaccine. No vaccine can be 100 per cent perfect when the disease itself does not offer complete immunity in many instances. It is not at all unusual to see a child have pertussis twice and perhaps have it twice within two or three years.

In estimating the protective value of pertussis vaccines, we should take into consideration the varying types of epidemics of pertussis—sometimes it is exceedingly mild and responds well to almost any treatment.

We have used the Krueger antigen considerably and concluded that it should be given frequently and in larger doses. Cases in children who were given the antigen within the first seven days of the onset of the cough were decidedly mild.

CHAIRMAN PARK.—How severe were untreated cases occurring during this time? Were they severe, or was the epidemic in the city one of mild cases?

DR. MUNNS.—We have not had a real epidemic—a fact which may indicate that perhaps these might have been mild cases anyway.

DR. COLE.—What do you consider adequate quarantine regulations?

DR. SAUER.—Children should stay on the premises three weeks at the minimum.

DR. MAURICE L. RIPPS (ELIZABETH, N. J.).—Although I have seen one boy who was vaccinated with Sauer's vaccine and contracted pertussis, this case was milder than that of his unvaccinated sister to whom he was exposed. Upon inquiry I found that one pediatrician in the neighborhood had four cases and another two cases of pertussis which developed four months after vaccination with the Sauer vaccine. It may be possible that the technic we are using is different, or it may possibly be in our type of vaccine.

Dr. Munns mentioned that he had had no complications from the Krueger antigen. I have used the New York Board of Health vaccine, and out of 76 cases only one child had an acute bronchitis lasting three days.

To give 5 c.c. of vaccine several times a day to the usual patient with whooping cough in private practice would not be practical since it occurs most frequently in the poorer families.

In a recent publication it was stated that children treated with the Krueger vaccine at first showed an improvement, but after twenty to twenty-four hours the disease became as severe as before, then gradually improved. My own experience has been similar.

DR. FRAWLEY.—In the short series of cases in which I used large doses of vaccine, 5 c.c. to each injection, we found that when the vaccine was given twice a day our results were better than when it was given once a day.

CHAIRMAN PARK.—What is your advice at present to a physician as to how many doses to give in treatment?

DR. FRAWLEY.—In private practice the problem of the expense is a very important thing. The vaccine costs $2.00 for 5 c.c. If the injections are continued for very long, the expense is considerable. But within a week the amelioration of symptoms is so striking and the results are so favorable that the cost is more than compensated for.

DR. SAMUEL P. WAINWRIGHT (BIRMINGHAM, ALA.).—I want to report on over 1,500 children who have been immunized in my district, 1,200 of whom have been immunized four months or longer according to the directions of Dr. Sauer, their ages ranging from four months to eight years. In this group, ten cases of pertussis have subsequently developed, only one child being younger than three years of age. The age of greatest mortality is up to three years.

DR. J. M. LEWIS (NEW YORK CITY).—In the autumn of 1933 we had an epidemic of whooping cough in the Infant Asylum, an institution caring for about 325 children whose ages range from two weeks to three and a half years. We inoculated small groups of exposed children with the New York City Department of Health vaccine. We started by giving 20 billions, 10 billions in each arm, but the reactions were so severe that it was decided not to continue with these large doses in our exposed groups but to restrict the group receiving 60 billions to about seventeen. One small group received 40 billions and another 20 billions. Control groups of children were observed in the various wards.

Thirty children were vaccinated, and twenty-five children served as controls. When the vaccinated group as a whole was considered without regard to the number of organisms inoculated, there was no significant difference in the incidence or severity of the disease between the inoculated and control groups.

DR. W. L. CHADWICK (GRAND RAPIDS, MICH.).—With the cooperation of the Michigan Department of Health, we are having the vaccine made from the freshly obtained cough plates on sheep's blood agar; the vaccine contains 10 billion bac-

teria to a cubic centimeter. The injections are made as follows: 0.5 c.c. on the first day, 1 c.c. on the fourth day, 2 c.c. on the seventh day, and on the fourteenth day 2 c.c. bilaterally. We found that this injection has not resulted in any serious local reactions.

In my own practice with something over one hundred immunizations after more than four months following the completion of the treatment, two children in one family came down with whooping cough.

DR. A. E. AMICK (CHARLESTON, W. VA.).—I should like to ask Dr. Sauer if during the course of immunization the patient is taken sick and we are unable to continue inoculation at specified intervals, what shall we do after two to four weeks? Shall we go back and give a complete immunization, or shall we go on from where we were forced to discontinue injections?

DR. SAUER.—If the interval is not more than one month, you could go along and finish up the injections and give an extra dose.

CHAIRMAN PARK.—I do not believe that ethyl alcohol fails to disinfect. For some years I had Dr. Zingher use the alcohol disinfection and Dr. Schroder use the boiling method in diphtheria toxin-antitoxin immunization. There were no abscesses with either, and they made thousands of injections.

Dr. Waldie, will you answer the question asked of Miss Mishulow about reaction?

DR. WALDIE.—We do not get severe local reactions except to the intracutaneous method. However, we do get constitutional reactions; in about 50 per cent the temperature will rise that same evening, sometimes as high as 102° to 103° F., but usually around 101° or 101.5° F. It recedes by the next day, and it stays down.

DR. TANYAN (CLEVELAND).—We are using the cough plate to determine whether a patient has whooping cough. Can we assume he hasn't whooping cough if we get negative plates?

How should we take care of the Sauer vaccine? Should we keep it cold at all times? Is there any danger of its deteriorating due to improper care?

DR. SAUER.—A negative cough plate, no matter how well exposed and no matter how suspicious the cough, does not exclude pertussis. It is only a positive plate that is of value.

Miss Mishulow, how long does it take a potent vaccine to deteriorate? Is it advisable for a doctor to carry such vaccine around in a bag? Would transportation from the manufacturer in New York to San Francisco cause deterioration? Would enough deterioration occur if that crate happened to be above a radiator?

MISS LUCY MISHULOW.—It will have to be only an opinion because I have not carried out experiments to determine what happens to vaccine when it is carried around in a bag, or pocket, or kept at higher temperature. In our experience with the testing of pertussis and pneumococcus vaccines, we found after five years in the ice box they were as potent in stimulating agglutinins in rabbits as they were when freshly prepared.

CHAIRMAN PARK.—I think it would be helpful for you to say a few words about cough plates—how much training a person must have to give fair results.

MISS MISHULOW.—That is very difficult to say. Anyone who has had experience can pick them out very easily, but it may take a long time before an inexperienced person would be able to differentiate them. We isolate typical colonies morphologically and identify them by means of serum. We have monovalent rabbit serums and have tried a number of influenza strains but found that they do not agglutinate with these serums.

DR. SAMUEL KARELITZ (NEW YORK CITY).—Dr. Sauer says he has had some children who were inoculated shortly after measles and could not be immunized. Has he or has anyone else studied to see how long after an acute infection such a person is in the negative phase, if you will, and cannot be immunized? I think that is important to know.

DR. LEWIS.—We inoculated about one hundred children at the Home with Sauer's vaccine about four or five months ago, and the reactions were definitely milder as compared with those obtained with the New York City Department of Health vaccine. We analyzed the blood and found the same count Dr. Sauer has found. I would like to know whether he has any further data on that point. He stated that, if he did get a leucocytosis with a relative lymphocytosis following vaccine, the type of reaction simulated that which is seen with whooping cough.

DR. SAUER.—If sheep's blood is satisfactory, the vaccine can be made so much cheaper. Getting human blood is quite an item of expense. I think the Michigan experiment should work out very well.

CHAIRMAN PARK.—Miss Mishulow, have you anything to say as to why our vaccine gives more reaction?

MISS MISHULOW.—I do not know unless it is because we have in our vaccine an added substance which is not contained in Dr. Sauer's; that is, we take special pains to prepare our vaccine so it will have a toxic substance on the basis that such vaccine stimulates a high agglutinin response. We have this substance in addition to the ten billion bacteria which is Dr. Sauer's concentration. For that reason our vaccine is stronger.

DR. DAVENPORT.—In this work that Dr. Denmarks is doing with the three hundred children in Atlanta, she has made white blood counts and differential blood counts on the majority of her cases, probably two-thirds of them, and those results are very closely parallel to the ones that you made in your test. They follow your results very closely.

DR. S. A. ROSE (STAMFORD, CONN.).—In view of the tendency you showed on your first chart for the intracutaneous method of administration to enhance the strength of the vaccine, would there be any particular objection to combining both the intracutaneous method with the intramuscular or subcutaneous method, using 0.2 c.c., which I think is the point beyond which Dr. Waldie said he got some slight necrosis? It might be the equivalent of giving a larger dose.

CHAIRMAN PARK.—Several vaccines were given that way, part intracutaneously and the remainder more deeply. I can see no objection.

The meeting was adjourned.

FIFTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

Panel Discussion on the Common Cold

Dr. L. W. Dean, St. Louis, Chairman.

Assistants: Dr. Yale Kneeland, Jr., New York, "Etiology"; Dr. Richard M. Smith, Boston, "Complications of Respiratory Tract"; and Dr. Borden Veeder, St. Louis, "Treatment."

CHAIRMAN DEAN.—Children with normal noses and throats do not often suffer from repeated colds. Bringing about a return to normal in a diseased nose and throat usually prevents colds. The nasal pathology may be due to allergic, nutritional, or endocrine disturbances; consequently every patient suffering from repeated colds should be studied from these standpoints. Various violations of the ordinary rules of hygiene, particularly abnormal dryness of the air in the home, will cause pathology in the nose that predisposes to colds. The three outstanding etiologic conditions of the nose and throat responsible for repeated colds are infected lymphoid tissue in the pharynx, deformities of the nasal septum, and chronic nasal sinus disease. The infected lymphoid tissue in the pharynx may easily be removed; correction of the deformities of the septum sufficient to meet the exigencies of the situation can readily be done; the eradication of the chronic purulent nasal sinus disease, however, is a very difficult problem. Whenever there is stasis in the nose or nasal sinuses, there is always infection. All the things mentioned as etiologic factors in the production of colds, that is, nutritional disturbances, endocrine disorders, allergic rhinitis, deformities of the septum, and adenoids, have a tendency to cause stasis of the nasal discharge with resulting infection.

If we could stamp out chronic purulent nasal sinusitis in infants and young children, we would be far more successful in our treatment of colds.

A good treatment for acute purulent nasal sinusitis in infants and young children is as follows: Bed rest, diet, pediatric care, drop 1 per cent ephedrine into the nose, wait twenty minutes, then drop 5 per cent fresh argyrol into the nose. If the nose is dirty, clean by suction, or if very dirty, by irrigation. Following suction or irrigation, use 5 per cent argyrol drops.

Treatment of chronic purulent nasal sinusitis: Eliminate allergic factors. Remove infected lymphoid tissue from the pharynx. Correct conditions blocking the ostia of the sinuses. Avoid nasal treatments except when there is stagnation of sinus secretion or during acute exacerbations, then keep ostia of the sinuses patent and the sinuses clean. Avoid too much use of vasoconstrictors. Resort to hygiene and outdoor play. Regulate rest and sleep. An abundance of sunlight and sometimes change of climate are indicated. Nutritional therapy is most important; vaccine therapy is often of great value. It is often necessary to continue this treatment for two or more years in order to get the best results. As long as progress is being made, the attack should be continued along conservative lines as indicated. Only very rarely do we attack the sinuses surgically. Orbital cellulitis or osteomyelitis of the bones of the face may necessitate operation on the diseased nasal sinuses. This may be required at as early an age as eight months. Or the pediatrician says that we must hasten the treatment to eradicate the sinus as a focus of infection in arthritis, heart disease, hemorrhagic nephritis, or other systemic conditions. The exigencies of the situation do not permit of prolonged treatment, and a simple opera-

tion for securing drainage and ventilation of the infected sinus is indicated. A canine fossa operation in children is never performed unless the bone of the fossa is necrotic.

The pH of the nasal discharge has been studied by Miss Buhrmester. The nasal secretion of a normal nose has a pH of about 7.5. In the beginning of a common cold with the appearance of the watery nasal discharge the pH increases. It may reach 8.4. The cytologic examination reveals desquamated ciliated cells and some neutrophiles. If the cold subsides in a few days, the pH gradually decreases and is normal at the termination of the attack. If, however, acute purulent sinusitis develops, the pH becomes less than normal. At this time many neutrophiles make their appearance in the nasal discharge. As the purulent sinusitis improves, this acidity of the nasal discharge decreases.

Many so-called common colds are acute allergic upsets. In the beginning the pH is more alkaline as in the cold. However, the cytologic examination of the nasal discharge almost always shows many eosinophiles, and sometimes there is a blood eosinophilia.

The difference between the pH in a cold and acute allergic upset is that in the former it returns in a few days to normal, 7.5, while in allergic rhinitis it remains alkaline for a much longer period. If purulent nasal sinusitis complicates the allergic rhinitis, again we have the pH less than normal. At the same time we find many neutrophiles in the nasal secretion in addition to the eosinophiles.

If Miss Buhrmester tells me that in a case of chronic rhinitis the pH is increased, I would consider the case to be one of allergic rhinitis until proved not to be.

In the same way an acid reaction always suggests infection. Cases of allergic rhinitis with pH below 7.5 are almost always complicated by purulent nasal sinusitis. Only two or three drops of nasal discharge are necessary to determine the pH by the microglass electrode method.

Laryngologists are becoming ionization conscious. In allergic individuals and in persons with nonallergic intumescent rhinitis who suffer from repeated colds, ionization influences the attacks of acute rhinitis. I have studied cases in which only one side of the nose was ionized. Six weeks after the ionization, the individual had a cold; the un-ionized side of the nose became blocked; the mucosa was reddened; there was an abundance of discharge; the ionized side remained dry, and the mucous membrane paler and dryer than normal; on this side the patient was symptom-free. In a patient who had both sides of the nose ionized and had had an acute nonallergic upset six months after ionization, the mucous membrane became reddened, only slightly swollen, there was a very slight discharge, and the patient had but little discomfort. In this case the effect of the ionization was disappearing. I would like to say at this time that I do not approve of ionization of the nose except as a last resort and then only in allergic subjects with marked diffuse intumescent rhinitis involving the turbinates, meatuses, and septum. Such persons suffer from nasal blockage, etc., made worse by exposure to cold, dust, moisture or by lying down. Repeated colds are the rule.

DR. VEEDER.—Do you feel there is a background of pathology before the common cold is acquired?

CHAIRMAN DEAN.—While such a premise would not apply to 100 per cent of the cases, I do believe every patient who suffers from recurring colds has pathology in the nose in the nature of a thickened mucous membrane, with a tendency to produce stasis of nasal discharge, which always results in infection. In our laboratory animals, anything that causes stasis of sinus or nasal discharge results in infection.

While it is possible to have a cold without nasal pathology, in every case of frequent recurrent colds there are pathologic changes in the nose which are most important etiologic factors in the cold. If the pathologic condition is removed, the repeated colds usually disappear.

DR. KNEELAND.—Dr. Dean has emphasized the pathologic and anatomic abnormalities which govern the severity and the repeated incidence of the common cold. I am going to review very briefly some of the work which has been done in regard to the etiology of colds. The first question is the one relating to the identity of colds in infants and young children and colds as seen in adults. One must, at the outset, confess that a good deal of the experimental work and clinical observation in this research has been done on adults, and a good deal of it is applied only by inference to infants and young children. However, I think none of us would disagree with the fact that the diseases, although they display certain clinical differences, are fundamentally the same, for it is a well-established fact that colds run through a given household, affecting infants and small children and adults at the same time. Those clinical differences seem to me to be minor ones. In the uncomplicated cold in a baby, there is likely to be a little fever; whereas that is not the rule in an uncomplicated cold in adults. In addition, infants and young children have a much greater predisposition toward infection of the middle ear. Similarly, perhaps, there is at certain ages in infants and early childhood what seems to be a heightened susceptibility to severe manifestations of upper respiratory disease. The fact, however, that this disease is readily communicable, or appears to be, from infants to small children to adults and the other way around would indicate the fundamental identity of the two conditions.

The second question which arises in connection with colds is: Are colds one and the same disease? In other words, is the common cold an entity, or it is not? There is a good deal of evidence that readily comes to mind indicating that the common cold is not an entity. As Dr. Dean stated, a pure state of hypersensitivity of the mucous membrane of the nose can, if the correct antigen is present, give rise to a syndrome which clinically resembles an acute common cold. Similarly, I think we would all admit that a low grade sinusitis can flare up in a way that entirely simulates a new and acute cold. There is an ancient observation that unequal chilling of body surface can produce congestion in the nose, and the name of the disease itself suggests that most people have thought for many years that colds were due to chilling of the body surface.

It must be admitted then at the outset that the common cold is probably not an entity in that every instance of nasal discharge represents the same thing. Generally speaking, however, when we speak of the common cold, we mean the acute disorder which occurs more seriously and is more widespread in temperate zones than in the tropics, which appears to come in waves, and which is most frequently seen in the cold months of the winter.

Having thus defined the disease under investigation, we must ask ourselves whether the common cold is in fact a communicable disease. This seems rather a silly question because most individuals would admit that it is possible to catch a cold from someone else who is suffering from a cold. On the other hand, it is well known that throughout the nineteenth century many shrewd clinical observers denied the communicability of colds and related the disease entirely to alterations in the body caused by various internal disarrangements and not to an infectious agent.

What evidence have we then that colds are communicable? I think perhaps the most clear-cut observation along this line was the one performed in Spitzbergen three years ago. Spitzbergen has a population of about 500 people, children and adults. For about five months during the summer, when the harbor is free from ice, it is visited at intervals by boats from the outside world. During these five or six months, when Spitzbergen remains in contact with the outside world, they have a certain number of colds in the native population. Three weeks after the ice formed in the autumn of the year when these observations were made, colds entirely disappeared. For the next seven months, the community was quite free from the

common cold. When I say "quite free," I do not mean absolutely free. There were, as a matter of fact, four colds during that period of time. Three of those colds occurred in the same individual. In no instance was there any evidence that those four colds were communicated from one individual to another, in spite of the fact that the climate of Spitzbergen is an extremely harsh one and the habits of the natives are such as would be regarded by us as extremely predisposing to colds.

The scientists who were examining this phenomenon followed the bacterial flora of the upper respiratory tract of the natives of Spitzbergen carefully throughout the winter months. They found in the autumn, when colds were still prevalent, that pneumococci, streptococci, and influenza bacilli could be readily cultivated from certain individuals. They also noted that after the common cold had disappeared there was no essential change in this bacterial flora; it remained about the same throughout the winter, and the pathogenic bacteria could still be isolated.

When the ice went out in the spring, the first boat to come into the harbor did not contain what appeared to be an active cold. Two of the seamen had colds a week before, but at the time they landed they were almost completely symptom-free. Nevertheless, within a short time after the arrival of the boat, 125 of the 500 native Spitzbergen residents had acute colds. Even aside from the various anatomic complications, the various pathologic, constitutional, endocrinologic, and allergic factors which unquestionably influence the clinical variety and severity of colds, it would seem from this one single observation conducted with great care that we can make certain generalizations about the common cold.

One is that it is a very highly communicable disease. Second, in any community small enough so that the disease might be said to "run out," it will disappear provided that no new agent or agents are brought in from outside. Third, I think we may say that the ordinary bacteria of the upper respiratory tract, even though they are known to be pathogenic, do not in themselves initiate colds, because following the outbreak of colds in Spitzbergen there was no alteration in the cultivatable bacteria of the upper respiratory tract and no new organism appeared to be introduced. I have gone into this at some length because I think its implications are so extremely significant in the work which is to follow.

The obvious inference from the standpoint of etiology is that one must look further than the upper respiratory bacteria for the primary cause of colds, and that has been done both in this country and abroad, as everybody probably knows. The first to study the possibility of the filtrable virus as the cause of colds were Kruse in Germany in 1914 and Foster in this country in 1916. Later on, negative results were obtained by other investigators. Since 1928 in New York City, in Baltimore, and in Indianapolis a large number of experiments have been done in the transmission of common colds by means of bacteria-free material derived originally from cases of cold.

It has been found that if one takes a susceptible human volunteer rigidly isolated from the outside world and inoculates him in the nose with bacteria-free material obtained by filtration of nasal washings from acute cases of cold, in 50 per cent or more instances, depending on the technic, that volunteer will develop an acute common cold which is in all essential respects similar to the common cold as observed in nature. These observations, which we have repeated a good many times and which have been confirmed by others, have led us to believe that ordinarily speaking the cause of the common cold is not one of the many visible bacteria, and not, fundamentally, some idiosyncrasy or dyscrasia of the individual, but a filtrable virus passed from one individual to another.

CHAIRMAN DEAN.—Ionization does nothing more or less than cause a shrinkage of the diffuse thickened membrane in the nose that you find in intumescent allergic rhinitis and intumescent nonallergic rhinitis. Persons with chronic in-

tumescent rhinitis suffer from repeated colds. If this swollen mucous membrane on one side of the nose only is treated by ionization and the person develops a cold within six weeks, the untreated side will actively discharge, and its mucous membrane will be swollen and reddened. The side that was treated remains symptom-free; the mucous membrane remains pale; it is not swollen; neither is there an increase in the discharge.

Does this suggest anything from an etiologic standpoint?

DR. KNEELAND.—There are wide variations in susceptibility to infection with the virus. It might well be that some peculiar physical chemical alteration has rendered an individual temporarily, less susceptible to virus infection. It is true we have been unable to tell whether an individual is going to be susceptible to experimental colds. We attempt to select individuals whose throats appear to be normal. Yet out of three individuals inoculated, it is comparatively uncommon to find three susceptible. Frequently one individual will get nothing. One will have a moderate cold, and the third one may have a cold of rather unusual severity. We know of no way of determining in advance which ones will be susceptible and which will not.

If one admits that the primary cause of the acute cold is the filtrable virus, I think the next question which comes to mind is precisely what rôle the pathogenic bacteria which we know inhabit the respiratory tract do play in connection with colds.

There have been a good many observations which have led certain individuals to believe that a single pathogenic bacterium can spread widely from one individual to another and give rise to acute colds. However, the Spitzbergen experiment which I have detailed to you is, I think, evidence against that. In any case, I think no one would disagree that these organisms must or should play some rôle, and we have been interested in studying the relation of these organisms to respiratory disease in infancy.

After seven years of taking nose and throat cultures on young infants, we believe that the sequence of events is something like this: In the very early autumn before colds have become extremely prevalent, one finds that the carrier rate of pathogenic bacteria is quite low. By pathogenic bacteria, we mean pneumococci of various types, Pfeiffer's bacillus, and hemolytic streptococcus. These we believe the most important secondary invaders.

After the first autumn outbreak of colds occurs, there seems to be a dissemination of these organisms, and they become more widespread. The first autumn colds are usually fairly mild, and there is comparatively little in the way of complications compared to what occurs later in the winter. As this dissemination of pathogenic bacteria takes place, renewed outbreaks of colds occurring perhaps in January, February, or March, at a time when the carrier rate is extremely high, take on more serious character, and all the complications which have been and will be discussed are seen in great abundance.

With the warm weather again, for some reason we do not understand, the carrier rate of these organisms begins to fall off so that by the summer it has reached its original low level.

Turning for a moment to a single experimental disease of animals which has been very carefully studied, we can find a situation which is somewhat analogous. I refer to the disease of swine influenza which has been completely worked out through the efforts of Dr. Shope in Princeton. It is a highly communicable disease of swine, which occurs in epidemics in this country, particularly the Middle West. From the bronchial secretions and the lungs in fatal cases of this disease one can cultivate a hemophilic bacterium which closely resembles Pfeiffer's bacillus. That organism when administered in culture to healthy swine has no effect. It disappears in a few hours from the swine's upper respiratory tract, and no evidence of infection is ap-

parent. If one takes material from an acute case of disease, either lung or bronchial secretions, and obtains a bacteria-free filtrate and gives that to a healthy swine one gets a mild disease, not apparently of great significance. The swine has anorexia and a slight degree of fever. That state lasts two or three days. Then he is perfectly well again, and the disease is not communicable.

However, if one mixes this filtrable agent with a culture of the hemophilic bacterium, so-called *Hemophilus influenzae suis*, typical and highly contagious field type of influenza results. Here is a disease that is highly communicable and serious only when an etiologic complex is involved, that is, a complex involving a filtrable virus and a bacterium.

Our belief is that in human respiratory infection a rather comparable mechanism may take place. The cold virus itself produces a self-limited and relatively mild disturbance; the more severe manifestations arise when it acts in conjunction with not one, but many, pathogenic bacteria widely disseminated throughout a susceptible population.

DR. VEEDER.—Do you feel the differences in the clinical character of epidemics of upper respiratory infection, or colds, as we see them from time to time depend upon the secondary invasion? At times we see large numbers of children with colds develop gastrointestinal symptoms. At other times we will have a large number of children who develop ear infections, which progress to mastoid disease; perhaps twenty or thirty of them are in the hospital at the same time. Another year there will be only an occasional case. Do you think this variation depends on the character of the secondary organisms?

DR. KNEELAND.—I certainly believe that the local complications such as otitis media and mastoid disease probably are influenced to a considerable degree by the type and character of secondary invader.

In regard to gastrointestinal disturbances, I am not certain. I have observed epidemics in institutions for infants which were not associated with any increase in the pathogenic bacteria I could cultivate and in which the carrier rate was extremely low. However, these disturbances were very widespread and were characterized by acute gastrointestinal symptoms, and apparently they ran through a ward with great speed. Twice I have noted this phenomenon. It has taken place at a time when there was a good deal of what was called influenza in adult communities. I wondered whether that was not a manifestation of a different type of virus disease.

DR. SMITH.—In lay parlance, the cold is frequently said to have gone down: in other words, developed complications other than in the head. It is well to bear in mind that under these conditions a single area is rarely involved and that if the cold extends downward there is usually involvement of one or more of the areas, either in the larynx, trachea, bronchi, or the lungs.

CHAIRMAN DEAN.—May I ask a question, Dr. Smith? Following lobectomy, the severed end of a bronchus may be exposed. Its lining may be studied by direct inspection. In such a case if the patient develops a cold, the lining of the bronchus almost immediately becomes reddened and swollen. You can tell by watching the nose what is happening in the bronchus. Have you any idea how this infection gets down in the lung so quickly?

DR. SMITH.—I should suppose we would have to assume that it is infection spread frequently by lymphatics or blood stream probably not by direct extension.

The extent of involvement is more or less roughly a measure of the severity of the infection although it is possible for a single area to be involved and still have a severe disease as we shall discuss later in relation to the larynx and lungs. When there is general involvement of the entire respiratory tract, the disease usually is given the name of the area in which the involvement is most severe, but it is important for us

to remember that the name in that instance represents only the essential or prominent point of disease and that other areas are also involved.

In relation to involvement of the larynx, there are several things that one should bear in mind: first, the seasonal occurrence of the disease. It is relatively rare in the warm months. Second, the age distribution—it is much more common under ten years of age, and usually in older children it is not as severe as in the younger ones. Pathologically we have not only the local inflammatory condition but superimposed spasm which complicates the picture very much and adds materially to the difficulty of treatment.

So far as the local inflammatory condition is concerned, there is frequently marked edema, and there may or may not be exudate, varying with the severity of the disease, and also in certain instances the formation of membrane. Membrane formation usually occurs only in the severe types of disease, particularly with infection due to the streptococcus, and it has to be differentiated from the membrane caused by diphtheritic infection.

There are several things in relation to the symptoms which are important. In the first place, the hoarseness which accompanies the infection of the larynx may go on to aphonia. Since we are interested in differentiating this from diphtheria, it is well to bear in mind that aphonia is usually earlier and more frequent in diphtheritic infections than in infections with other organisms. In strepococcal infection the dyspnea is usually out of proportion to the hoarseness ranging directly with pathologic process. This dyspnea may be so severe as to be obstructive, and usually in cases that are most severe this obstructing dyspnea comes on very rapidly. The cough associated with the laryngitis is frequently paroxysmal in character, painful, and extremely difficult to control, particularly if there is also a good deal of involvement of the trachea.

So far as diagnosis is concerned, we have only to differentiate from diphtheria. I have already spoken of the relation between hoarseness and dyspnea, usually the absence of aphonia, but we can never be absolutely sure except by direct examination with culture. The presence of a negative Schick test is of considerable value.

It is not necessary to discuss in detail the treatment of this condition, but there are one or two matters which I should like to mention. In the first place, we must remember we are dealing with a general infection and that the general infection, as such, needs to be considered. The regulation of the temperature or atmospheric conditions under which the patient is placed is also very important. The temperature of the room should be as nearly as possible of a uniform degree, warm but not too hot. The air should be moist. Frequently the addition of some substance to the steam used to produce moisture is desirable. It is, however, important to remember that benzoin, which is the substance frequently used for inhalation, is irritating to certain individuals and may make the condition worse.

Local application of cold to the exterior of the throat is efficacious in controlling cough in many instances. We usually depend, however, upon sedative drugs. It is to be borne in mind that if these individuals can be prevented from talking and coughing, their difficulty will be very much less. Occasionally mechanical relief is necessary, either by intubation or tracheotomy. It is important to emphasize that one should procrastinate as long as possible before the employment of mechanical means for relief, because if we procrastinate long enough, we frequently will be spared the necessity of introducing any mechanical feature.

CHAIRMAN DEAN.—What influence does the presence of adenoids have on the development of laryngitis in an individual who has a cold?

DR. SMITH.—I would say that directly there is no relationship, but indirectly, considerable, by preventing free breathing through the nose; in other words, the inhalation of air through the mouth may cause more difficulty.

DR. VEEDER.—Do you feel that if the adenoids and tonsils are taken out, there is likely to be more laryngitis and tracheitis?

DR. SMITH.—You mean in subsequent infections? I would not say so, but I might stop and ask a question of Dr. Dean in that connection. If we take out the adenoids and tonsils, are we more likely to have infection in the sinuses as a secondary complication?

CHAIRMAN DEAN.—I think not. However, there is a decided difference of opinion in this matter. I do not know of any series of children that have been studied from the standpoint of the sinus pathology before and after the removal of infected lymphoid tissue from the oropharynx and nasopharynx. A number of groups have been studied after this tissue has been removed, but there is no record of the condition of the sinuses before operating.

Sinus infection produces certain changes about the nose and throat that often hasten the removal of infected lymphoid tissue from the pharynx. In some cases it is responsible for the acute infection of the pharyngeal tonsil. Many of these patients in whom sinus trouble was diagnosed after the operation on the throat have had the infection before the operation. I am convinced that the removal of adenoids will not have any deleterious effect on the nasal sinuses. I am so convinced of this that my own grandson eighteen months old, on the advice of pediatricians, had his adenoids removed. I think without any question whatsoever the removal of his adenoids will not have any bearing upon the child's developing sinusitis. It is interesting to note that, while before his adenoids were removed, he had many colds during the fall, winter, and spring, after the removal of his adenoids the mucous membrane of his nose was thinned, and in one year he has not had a cold, even when all the other members of the family were affected.

DR. SMITH.—Do you feel equally strong about that with reference to the tonsils?

CHAIRMAN DEAN.—We have in the upper respiratory tract, the lingual, the palatine, the pharyngeal tonsils, and the infratonsillar nodes. I think taking out the bulk of this lymphoid tissue at the age of two years or younger is something to be avoided. However, if the palatine tonsils are infected and the infection cannot be controlled and is producing deleterious results, they should be removed. In such tonsils the microscopic preparations show that the bacteria are entering the lymph stream. The microscopic examination is convincing evidence that the tonsils should be removed. Certainly if an infant suffers from repeated attacks of acute follicular tonsillitis and with such an attack he develops bronchopneumonia, the palatine tonsils should be removed at a proper time. The lingual tonsils, the infratonsillar nodes, the small lymphoid masses in the posterior wall of the pharynx remain and are capable of carrying on any necessary function. Certainly in the few infants in whom it has been necessary to remove palatine tonsils between the ages of eighteen and twenty-four months, I have not noticed the development of nasal sinusitis. Neither do I expect it to appear as a sequela of the operation.

DR. SMITH.—To come back to the infection of the larynx—there is a form of this infection which perhaps deserves special mention, the severe type of laryngotracheobronchopneumonia. We use all the names because we recognize that from the onset the disease is not localized in any particular area but is a general infection. It is to be noted that this condition rarely, if ever, has a gradual progression from the milder form of the disease. There may be a slight cold for a few hours, but

its onset is sudden with high temperature, rapid pulse, prostration, and severity from the beginning. It is relatively rare in infants and has a high mortality. Pathologically it is usually a streptococcic infection. The lungs are always involved; there is often a septicemia. There is extensive exudate in the larynx and trachea, extending frequently into the smaller bronchi. This gives rise to a tenacious secretion, forming a hard membrane, frequently casts of bronchi, which are difficult to expel by coughing.

Here again the treatment is of particular importance, and the treatment of the general infection is to be primarily considered. So far as the preliminary procedures are concerned, they are the same as in simple laryngitis, but mechanical relief is much more likely to be necessary. This consists of suction, intubation, which is particularly ineffective when there is edema above the glottis, and more often tracheotomy.

Through the tracheotomy wound it is necessary by suction to remove the hard membranes which produce mechanical obstruction enough to endanger life. It is to be remembered that however successful we may be in relieving the dyspnea and mechanical condition, these children are sick from a general infection, and they may, and I think usually do, die of the general infection as often as from the mechanical condition. The mechanical condition presents an emergency complication which requires specific treatment, but one is dealing in the first instance with a severe disease with a high mortality.

Complications which occur primarily lower down in the trachea, the bronchi, and the lungs will be presented only very briefly. Tracheitis rarely occurs alone and is often associated with a slight bronchitis. The thing one has to bear in mind with infection of the trachea is that there may be a very stubborn, severe cough which is hard to control.

It is important in infections of the bronchi and lungs to remember that an allergic background very materially changes the character of the picture. Asthma, so called, may be superimposed upon the infection. It is impossible to differentiate in many instances what is called a capillary bronchitis from a true pneumonia.

So far as pneumonia is concerned, in this condition we are dealing with a secondary pneumonia, which in children has a more grave prognosis than primary pneumonia.

In the diagnosis of this condition it is important to remember that even a severe infection in infants may be afebrile but usually is accompanied by an elevation of the white blood count. The physical signs are often inconclusive and the x-ray is of real value in determining the extent of pulmonary involvement.

The complications of these infections in the lung beyond the pneumonia itself are several. Sometimes with marked enlargement of the mediastinal glands one may have enough obstruction to produce emphysema. In the course of healing, the lung may return to normal, or it may fail to do this and develop an abscess, bronchiectasis, or a chronic pneumonitis recurrent in nature.

DR. VEEDER.—When Dr. Dean asked me to discuss the treatment of colds, I told him quite frankly I did not know much about the treatment of colds, and I do not know any one who does. We may divide the treatment of colds into two phases, the treatment of acute cold itself and the prevention of colds. We have to consider, as was brought out here today, three different things when we speak of prevention of the common cold: one is that beyond question it is an acute, highly contagious infection due to a virus; second, that the chief troubles we see coming from colds are probably due to secondary invasion; and third, that pathologic changes in the nasal mucous membrane, as Dr. Dean has discussed, play an important part in the recurrence of colds.

In regard to the question of prevention, there are only a few things that are important: first, we know there is a gradual development of a certain degree of immunity. Epidemiologic studies show that the average individual has about three colds per year. In children under the age of five years, the frequency increases very much. Furthermore, the younger the individual the more dangerous the cold and the more likely are complications to develop. Therefore, it would seem that the most important thing in the prevention of colds is avoiding exposure particularly among young children. I need not go into the great stress we place on the prevention of colds in our hospital work—that is, the isolation of children with respiratory infection—because we know it has reduced both morbidity and mortality.

Many ideas have been expressed about the prevention of colds. A great many believe an individual can be hardened so that he will not be so susceptible. There is no proof of this. As a matter of fact, the few studies which have been made of the effect of hardening have shown that the individual hardened by baths and open air had as many colds as those who sleep with windows shut.

DR. SMITH.—What do you think about the coddling process as contrasted with the hardening?

DR. VEEDER.—I think the coddling is overprotection, softening rather than hardening.

The question of diet comes next. We have not the slightest evidence that any of the special fancy diets advocated, as omitting carbohydrates, has any influence. Dr. Davis studied her group in Chicago for two or three years and found the diet had no influence. There is no scientific evidence which I have been able to find that indicates that vitamins are of the slightest influence in preventing common colds.

Irradiation is another method which has been tried. A few years ago most doctors had to have a radiation machine of some type or other in their offices. Since the studies of Barenberg, Colebrook, and others have shown that individuals who receive regular radiation over a period of many months in a year have the same number of colds as those not radiated, I think we can eliminate that.

The question of vaccines is most interesting and difficult about which to form much of an opinion. Some people feel they get good results from the use of vaccines. Others are positive they are of no value. I think this matter is fairly easily explained. We cannot apparently vaccinate against the virus infection, but we do vaccinate against the secondary invaders. If we happen to inoculate against the organisms which were present in the community at a certain time, we will probably get a good deal of protection against the serious secondary results of a cold so that the cold becomes a very simple thing which is passed over in two or three days. If, on the other hand, we give half a dozen organisms in our vaccine, and it does not happen to contain the organism which is present in that peculiar wave of invasion in the community, the vaccine is probably of no value. Certainly some of the work Dr. Kneeland has done and also the work of Dr. Stollenburg, of Denmark, indicate that vaccines may be of value. The latter had five times as many infections among the unvaccinated as among the vaccinated children. In other words, vaccination probably will protect against the secondary invaders.

DR. SMITH.—If you use stock vaccine, what organisms do you include in your vaccine?

DR. VEEDER.—I feel personally that I have little use for vaccines, and I use them very little. I sometimes give them and occasionally see good results. The thing from which to judge is a controlled series rather than individual impressions. Those series have been made up largely of subjects inoculated with vaccines made from organisms collected in a community at a specific time, organisms which are prevalent in the community.

DR. SMITH.—Is it not true some of the individuals who are enthusiastic about the use of vaccines believe their results are exactly as good from a stock vaccine made from a number of organisms, as the results from autogenous vaccines?

DR. VEEDER.—Some do, and they may happen to hit it in the stock vaccines. It depends on whether the stock vaccine contains the organism which is a secondary invader.

DR. KNEELAND.—I must say I heartily applaud everything Dr. Veeder has said so far, particularly the remarks about the use of ultraviolet and hardening processes. In regard to vaccine, I think my own experience is exactly in accord with what he said. We used a vaccine made up simply of Pfeiffer's bacillus, hemolytic streptococcus, and pneumococcus, giving injections over an unusually long period of time at weekly intervals, and found no reduction in the number of individual respiratory infections in the vaccinated as opposed to the control group.

We did find the duration of fever was materially altered; the vaccinated group had, during the height of the season when respiratory diseases are prevalent, less than half as many days of fever due to respiratory disease as the control group; and this fact we took as a rough measure of severity of the infection. We thought we had modified the severity but had not in any way modified the incidence.

CHAIRMAN DEAN.—Dr. Kneeland, do you think the use of vaccine favorably influenced the mild chronic infection which was present about the upper respiratory tract?

DR. KNEELAND.—I think it did. There were fewer severe complications in the vaccinated group. Were I doing that again, I should perhaps do it a little differently in regard to the question of the type of organism. I have made up some vaccine in the past two years which has been used a little here in New York by a few pediatricians. Some of them have reported that in the extremely susceptible child they felt it had modified the severity considerably. I simply took so-called stock "cold vaccine" and added to that Types 6, 14, 19, and 23 pneumococcus. In my experience those are the four types having the closest association with upper respiratory disease in infants.

DR. VEEDER.—I think there are some ten thousand references to the common cold in the literature, and I assure you I have not gone over the ten thousand. The most interesting thing that has come up in the last two years is the preliminary report of some work done in California on air-conditioning in relation to prevention. Kerr and Langan in California in 1934, air-conditioned a large room, regulating it with filtered air at 70 or 71° F., with relative humidity of 55, and an air flow of 66 cubic feet per minute. They took several groups of individuals susceptible to colds and kept them in the room for four or five days in order to be sure the subjects were not developing colds over this period of time. When the investigators felt the subjects were free from the infection, the investigators introduced an individual with an acute cold. In the first three experiments, putting an individual with acute infection in with the individuals susceptible to infection, the susceptible individuals did not contract any infection. Kerr and Langan followed out the experiment further and had the subjects all use the same thermometer. Still those who had been in the air-conditioned room for several days did not contract colds. With the final group the experimenters took the washings of nasal secretion and put the washings on the mucous membrane of the susceptible subjects and found even then they could not transmit the cold. These experiments tend to show that the common cold is not transmissible in an environment arranged for maximum comfort. We must keep in mind that these subjects were at rest. As far as the prevention of cold is concerned, it seems we have a very easy solution. All we have to do is to air-condition our homes, and then arrange all our lives so that we need never go out of our homes.

CHAIRMAN DEAN.—I would like to ask Dr. Veeder a question. If we assume for purposes of discussion that a thickened membrane in the nose is an important predisposing factor to colds, what bearing would the controlled air experiment have on that theory?

DR. VEEDER.—My answer would be only an opinion, but I would feel that any individual, as Dr. Dean brought out, who has developed pathologic changes of the mucous membrane must have that put right in order to prevent further infection.

The second point of my discussion relates to the treatment of the cold itself. I think one can simply say one has to treat the common cold the same as any other infection, put the individual at rest under as good conditions as possible. That will probably prevent the development of many secondary infections and shorten the course. I believe every drug in the pharmacopeia has been tried. There is only one drug regarding which I think there is the slightest evidence that it is of value. I personally feel it is of a great deal of value. I refer to opium in some form. I think many a cold may be shortened if at the very beginning a big dose of opium is given.

I think the most harmful procedure is the constant flushing out of the nose with all sorts of antiseptics. I do not believe you can influence the bacterial growth or virus infection at that stage with any antiseptic. If one does anything, it should be simply keeping the nose clear by the use of a normal saline solution. If you have to put something into the nose, and you stick to saline solution, it may not do much good but it will do less harm than has been done in the past by pouring medicated nose drops down the nose of every infant and child who has a sniffle.

CHAIRMAN DEAN.—We will now proceed to answer some of the questions which have been submitted.

QUESTION.—Is there any relationship between the type of organism found in the culture from the nose and the form of complication in the ear, sinuses, glands, and so forth?

DR. KNEELAND.—I believe a rough relationship exists, although I have never been able to define it exactly in my own mind. It seems to me that cases of cervical adenitis are more frequently associated with the presence of hemolytic streptococcus in the throat than any other organism. Similarly there are certain outbreaks with a fairly high incidence of pneumococcic infection which seem to be characterized by otitis media. On one occasion, we observed a very severe outbreak of pneumonia which had a remarkably high mortality in an infant ward. In that outbreak we found Pfeiffer's bacillus was almost universal in that group of children.

QUESTION.—Is it safe to assume in a population of 500 there must have been some previously existing nasal pathology and such pathology has no relationship to the incidence of cold or the eradication of such pathology for cold prevention?

DR. KNEELAND.—That is rather difficult to answer. Perhaps if it could be traced, no absolutely essential and primary relationship could be found.

QUESTION.—If a cold is due to a virus, why does not the individual develop an immunity?

DR. KNEELAND.—I think he does develop a short immunity in most cases. The obvious indication of this question is: If this is a typical filtrable virus disease why should not the attack confer lifelong immunity like smallpox? Other well-established virus diseases like foot and mouth disease of cattle and the ordinary herpes simplex of man are certainly virus diseases. They confer a very transitory immunity.

Why cannot it be said that instead of a filtrable virus you have by a change in the climatic condition or temperature a better culture medium for the germs

usually present in the nasal passages? We have managed to cultivate this virus in the manner derived originally by the making of the cultivation of vaccine virus, except that anaerobic conditions are reversed, being passed along from one batch of medium to another for an indefinite period of time, still retaining its activity.

If that material perhaps in one one-hundredth subculture from the original washing is given to a suitable volunteer, he will contract a cold. You might say you were altering the condition of his culture medium, permitting his own bacteria to function. If you heat that to 80° for half an hour it surely could not alter very greatly. From a physical chemical standpoint, it is bound to be inactive. I think the evidence is very favorable in the direction of a filtrable virus.

QUESTION.—Does the erupting of one or more teeth heighten the susceptibility to a common cold?

DR. KNEELAND.—This question is somewhat out of my line. My impression is that teething often produces congestion in the nose and stems somewhat the nasal discharge and under those circumstances probably susceptibility to infection is increased.

QUESTION.—I was interested in one thing Dr. Smith pointed out: that is in the question of tracheotomy whether to look at the problem as a general rather than as a purely local one.

DR. SMITH.—I think we are prone to be so concerned about the obvious mechanical difficulties of breathing that we look upon the severe cases of laryngitis as primarily laryngeal infections, when, as a matter of fact, they are general infections, septicemias. There is almost always involvement of the lungs as shown by examination before death, and invariably the patient who comes to autopsy shows general involvement. We ought to think primarily of the treatment of the general infections and not allow ourselves to be concerned alone with the relief of mechanical obstruction.

QUESTION.—Do you think the administration of an alkali is valuable in checking the advancement or severity of the common cold?

DR. SMITH.—No. I do think the administration of alkali frequently gives relief when there is a profuse nasal discharge which is irritating. If one gives a considerable amount of alkali, one may reduce the irritating quality of that discharge. As far as my own feeling is concerned, I do not believe it modifies the course of the disease in any way.

QUESTION.—Why do the lung changes and those in the nose and throat so often go together?

DR. SMITH.—I think because of the fact which we have just mentioned in relation to these severe conditions and which is undoubtedly true to a lesser degree in the milder conditions: that the disease is almost never localized to one particular area of the respiratory tract.

QUESTION.—Does hypofunction of the thyroid predispose to colds?

DR. VEEDER.—I have no information on the subject and can only hazard an opinion. I do not believe it does.

QUESTION.—What effect has meteorologic conditions on the incidence of colds?

DR. VEEDER.—Probably changes in humidity have a relatively greater effect than changes in temperature.

QUESTION.—What do you think of the advantage of group play as against the danger of contact infection?

DR. VEEDER.—I feel one has to balance in the individual child whether the danger of infection or the danger coming from maladjustment or lack of social contacts is the most important. I believe the nursery school has a very definite, but a very limited, field. I would much prefer to keep a child out of the nursery school unless he were developing social problems that I felt could not be corrected in any other way.

CHAIRMAN DEAN.—We have a number of questions about ionization. The indications for and against its use are not as yet understood. We need to know more about how it acts. Certainly it should be used only after a very careful immunologic study of the patient has been made.

QUESTION.—What percentage of your patients have normal anatomy and normal mucous membrane in the nose and upper respiratory tract?

CHAIRMAN DEAN.—In St. Louis, in spite of sulphur gases in the air, we see many people with no pathology of any clinical significance about the nose and throat. About 15 per cent of the patients referred by pediatricians and internists for examination have no pathology of clinical significance.

QUESTION.—What percentage of eosinophiles in the nasal discharge indicates allergic origin of the cold?

CHAIRMAN DEAN.—That is something you have to decide by knowing your normal. In allergic rhinitis, the eosinophiles are grouped, and when you find a group of eosinophiles, particularly if they are exploding, it suggests allergic rhinitis. The increase of eosinophiles does not make the diagnosis.

Another question is: Do they leave after the attack? Decidedly no. We have children who have had acute allergic rhinitis in 1927 or 1928, and on allergic treatment they have remained symptom-free. Up to this date they still have the bloody eosinophilia and have numbers of eosinophiles in the nasal discharge in spite of the fact that there are no allergic upsets.

QUESTION.—As to the use of argyrol, why not use 10 per cent?

CHAIRMAN DEAN.—The only reason for using the 5 per cent solution is that 10 per cent argyrol does not keep well. It deteriorates easily. The 5 per cent solution does not.

QUESTION.—Does the use of argyrol interfere with the ciliary action?

CHAIRMAN DEAN.—The use of argyrol in experimental animals demonstrates that it has no significant action in slowing down ciliary action.

The action of drugs on the ciliated cells is important. Equally important is their action on the mucus of the nose. Covering the mucous membrane of the nose is a layer of mucus. The lower stratum only is directly driven by the cilia. The upper stratum is pulled along by the movement of the lower. Anything that changes the viscosity of this mucus, drying or the use of fluids, interferes with the movement of the surface of the mucus. The cilia may be working perfectly, but the surface mucus may be at a standstill. Any substance used in the nose that changes the consistency of the mucus has a deleterious action.

Dr. Veeder said drugs should not be used in the common cold. I would say surely not. We have not used any kind of medication for years in the nose unless there is some evidence of the blocking of a sinus opening. Then one should do something to keep the ostia of the sinus patent because good drainage is an important thing in the prevention of sinusitis. The moment acute purulent sinusitis develops one should resort to a certain amount of medication, but even then it must be used just as sparingly as possible.

FORTY YEARS OF SCHOOL MEDICAL INSPECTION

Report of the Committee on School Health of the American Academy of Pediatrics

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SCHOOL medical inspection in this country is forty years old and yet it still retains the painful and awkward growth of early adolescence. Its inconsistencies, its sentimentality, and its sometimes boastful claims have caused doubt about its ever growing up. A brief review of its developmental history is proposed to see if we may discover early signs of maturation.

THE BEGINNING

Physicians were first employed in the public schools of Boston in 1894 as a means of controlling a diphtheria epidemic. Philadelphia followed in 1895 and New York City in 1897. This service was limited to the inspection of children referred by the teachers because of suspected contagious disease.[1] In 1902 New York City provided a routine inspection of all children to detect contagious eye and skin diseases. These inspections revealed 20 per cent of the children with trachoma, 70 to 80 per cent with pediculosis, 10 to 12 per cent with scabies and ringworm and not infrequent cases of favus, impetigo, and wounds of various kinds. When 300 were excluded in one school in one day, this problem became acute, and the service of the first nurse in the schools was tried—the first municipal nurses were employed in New York City. The control of contagion and prevention of absences thus characterized the beginning of school medical inspection.

EARLY GROWTH

In 1905 New York City began a new era of school medical inspection with the examination of each child to determine the presence of noncontagious physical defects.[2] The next ten years was a period of rapid growth and of development of programs of examination, inspection, and follow-up of physical defects in most of the large cities of the country. It was also a period when a few educational and public health leaders pointed out the possibilities of a well-rounded school health program which included supervision of the school plant, physical education, health education and supervision of the hygiene of instruction. In 1914 Hoag and Terman[3] proposed "health and development supervision" in the schools as an educational program which included within its scope almost everything which contributes to the conservation of the child. The writings of Leonard P. Ayers, Luther Gulick, Fletcher B. Dresslar, Walter S. Cornell, Louis W. Rapeer, and many others of this period showed a recognition of the problems of school hygiene, proposals for organization, and plans for future development that have been realized only to a small degree in the twenty years that have followed. The reports of the Fourth International Congress of School Hygiene at Buffalo in 1913 showed a vision of the possibilities of hygienic supervision of all school activities and of medical and nursing service and health teaching that is as comprehensive as any of the present day.

Prepared for, revised by, and approved by the Committee on School Health of the American Academy of Pediatrics: Dr. LeRoy A. Wilkes, Chairman, Dr. H. H. Mitchell, Dr. R. M. Kempton, Dr. M. Hines Roberts, Dr. A. C. Silverman, and Dr. C. D. Sweet.

Ninety cities were reported as having medical inspection in 1907, 337 in 1910, and as many as 500 by 1913, although it was then recognized that a great amount of the service could be called health work only by courtesy.[4] In 1911 Gulick and Ayres[5] reported 69 per cent of over 1,000 city school systems had some sort of medical inspection.

THE ADVENT OF THE SCHOOL NURSE

The advent of the school nurse resulted in a similar rapid increase in the number of cities accepting this service. By 1911 there were 102 cities employing a total of 415 school nurses according to the survey of the Russell Sage Foundation. By 1913 New York City had 176 school nurses. Studies in both New York and Philadelphia indicated the improved results in obtaining care of contagious diseases and in the correction of physical defects through the follow-up of the school nurse. The value of the nurse in the school was so much appreciated that many cities employed nurses without the services of a physician. Louis W. Rapeer, who had studied medical inspection in about 40 school systems, came to the tentative conclusion that many schools do not need physicians and that a great deal would be gained and little or nothing lost by employing experienced school nurses for each group of 1,000 to 1,800 pupils.

STRUGGLE FOR RECOGNITION OF HEALTH IN THE SCHOOLS

The period up to the time of the revelations of the World War draft was characterized by more and more communities employing more and more nurses and physicians. Nurses were taken directly from hospitals or private duty with no special training to serve in the schools without qualified leadership or supervision. Physicians were employed to examine and accumulate huge records of physical defects. The problem of minor contagious disease was put under control, but the big hope of improved health and correction of physical defects failed to meet expectations.

This was a period of struggle for recognition of health in the educational program of the schools. The preventable disease which caused absenteeism and the physical handicaps which interfered with school progress gained recognition as problems requiring the expert assistance of the physician and nurse. Low salaries and lack of training for this new field of work seriously handicapped the development of effective service for meeting the need. When the service was under health department control, there was too often a shortage of funds and political interference, and when under the education department control, the direction of the service was too often left to busy private medical practitioners who did not have time to study the problem or to give the supervision necessary for efficient service. A few medical and educational leaders, no doubt, had visions of "hundreds of researches" out of which "a new science of educational hygiene" should arise, but these dreams failed to materialize.

IMPETUS OF THE WAR

A new impetus to school health program improvement came out of the movement for conservation of human resources which accompanied the wartime patriotism. A small group of physicians, social workers, and educators organized the Child Health Organization of America and popularized a new health education. The late L. Emmett Holt, who gave much thought and leadership to this campaign, pointed out that "the school is the place where health instruction must be given to most children if they are to get any proper health instruction."[6] He outlined two kinds of health instruction: one relating to matters of public health and one concerned with the promotion of health through good health habits. He emphasized that "the child can easily learn the essential needs of his body, such as proper food, cleanliness,

fresh air, exercise, rest, regular bowel movements, etc.,'' and he said, ''It is self evident that before children can be influenced they must be interested.''[7]

THE NEW HEALTH EDUCATION

This new idea in health education spread rapidly aided by such popular devices as Cho Cho the Health Clown, the Health Ventriloquist, the Health Fairy, the Jolly Jester, plays, games, booklets, a series of attractive pamphlets and the campaign for scales in every school. The campaign of weighing and measuring was a scheme to interest the child in a competitive game with rules that required the practice of health habits. In 1921 Holt wrote, ''The value of the class room weight record distributed through the Bureau of Education by the hundred thousand is very great in influencing the child, because weight is something concrete, the significance of which his mind can grasp.'' Under the influence of effective promotion most schools accepted the zone of normal weight as a criterion for determining the condition of nutrition—''the best general index of health.''[8] Underweight children were put in nutrition classes all over the country and many a parent became interested in health habits and good nutrition. But the child who failed to attain normal weight was not always accepted as malnourished, and the search continued for better tables of weight. This period was characterized by a search for better standards of health and nutrition. Many conferences and studies sought to determine a new scheme to measure nutrition and health and to select by measurement methods the undernourished child. The intensive educational and follow-up service for the underweight children demonstrated the possibilities of the new health education. But the lure of the overly simple weight for height criterion of nutritional status delayed progress in the development of examinations and sound medical advice for all children during the postwar period.

The constructive discovery that came from this promotion and expansion of the health program was early emphasized by Holt when he said, ''We cannot too strongly emphasize the fact that the essentials of personal health are such simple things as these (referring to health habits) and that even the untrained teacher, once she is interested, can carry them into effect.'' The new health education in the schools with its emphasis upon health habits, and attitudes was a distinct contribution of this period. Education for health behavior as a way of personal and social living became a new ideal to be achieved through all the child's experiences in healthful living. The realization spread that ''the hygiene that has been taught has been too general and abstract and has aimed at knowledge rather than health ideals and practice.'' The old textbook hygiene was summed up by Dr. Richard Cabot as, ''the yellow dog among the studies of the curriculum.''

THE IDEAL OF MEDICAL HEALTH SUPERVISION

Along with a new ideal in health education there developed the ambitious objective of complete annual health examinations for every child and medical health supervision that went beyond all possibility for fulfillment in the school. This was the period of promotion of the health examination idea. The advertising of the Life Extension Institute, resolutions of medical societies, and propaganda of public and voluntary health agencies, all tried to convince the generally indifferent public of the value of the health examination. The promotion of the health center idea by the Red Cross and other agencies during this period was based on the hope of providing such individual preventive pediatric service through coordinating various social forces of the community. The Cambridge Health Education Conference adopted the following recommendation regarding the physical examination of school children:[9]

"I. The aim of such an examination is to provide for every child a chance to achieve the limit of his endowed capacity for well-being.

"II. The function of the school physician should be:

1. To provide guidance toward better health through education of the children.
2. To provide an examination service which (1) discovers all physical defects, diseases, incipient conditions and tendencies toward ill health among school children, and (2) finds sources for remedy."

Indeed, the medical service in the schools was given ambitious ideals.

Such superior school medical service was demonstrated throughout the country in nutrition classes in which selected groups were given special training in health education, intensive follow-up by nurses, and medical service as thorough and complete as preventive pediatrics could supply.* These fine demonstrations were guided by a few selected pediatricians and revealed the possibilities of medical health supervision of a few children. They raised hopes of a school service for all children beyond the possibility of attainment. Since the few pediatricians could not continue to demonstrate *indefinitely* nor extend their services gratuitously to all children, the health education and follow-up was attempted without the physicians' services.†

The children 10 per cent underweight were labeled undernourished, milk was given them in school, some were required to take extra rest; many had their tonsils taken out; and it was supposed that the essentials of the health program had been preserved. The reaction came. The demonstration was over, and the schools had developed neither a thorough health education program nor a better grade of medical examination.

CONSENSUS OF OPINION FAVORS CENTRALIZED SUPERVISION

Another idea which received considerable attention during the period of rapid extension of school health activities was the need for administrative supervision of the numerous aspects of the school program which contribute to health and health education. Most of the writers following the period of rapid extension before the War recommended a trained full-time director of the health program to supervise and coordinate health education, medical and nursing service, dental service, physical education, mental hygiene, sanitation of the school plant, and supervision of all aspects of the curriculum which affect health. They recognized the importance of supervision, training of personnel in service, the improvement of morale and the correlation of all services into a well-rounded program. They anticipated the development of a new kind of health administration with an administrator trained in education as well as child health. This emphasis upon adequate direction, promotion, supervision, and coordination has been repeated again and again by practically all the educational and public health leaders for twenty-five years. The National Child Health Council in 1920, through much committee activity like that of the Hoover White House Conference, developed the consensus of opinion of that year, and their

*The Joint Committee on Health Problems in Education of the National Education Association and American Medical Association report from a questionnaire survey in 1922 that 54 per cent of 309 cities report nutrition classes, and the Research Division of the American Child Health Association in 1923 and 1924 showed 40 per cent of eighty-six cities had nutrition classes

†The Joint Committee Survey reported that in 24.8 per cent of the cities the school nurse conducts nutrition classes and the school physician and school nurse conduct them in 11 per cent of the cities. The same survey showed 83.4 per cent of the cities were weighing their pupils and 52.2 per cent of the cities weighed them as often as four times per year or more; 42.8 per cent reported monthly weighing. The American Child Health Association survey three years later seemed to indicate some loss of enthusiasm for the frequent weighing as 38 per cent were weighing as often as three times per year or more, and 27 per cent monthly. In 1930 the United States Bureau of Education Survey suggested that nutrition classes and supplementary feeding appeared to be decreasing.

report gave particular emphasis to the importance of such an administrative set-up.[10] And yet few schools have developed this kind of an organization. With the repetition of the importance of such direction by the White House Conference, it appears clear that the consensus of opinion leaves no question as to the need for school health programs of cities and other administrative units to have a centrally supervised and well coordinated organization.

SIGNS OF MATURATION

We have seen the rapid growth of the infancy and the early childhood of school health programs and then the long period of added increment in size with very few clear indications of the characteristics which the adult form will assume. The many public leaders who have contributed to the growth of this youngster have been impatient because of their desire to know just what a fully grown American school health program would look like. With the first signs of maturity we see that some of the development during the steady growth period was sound and is likely to persist as an effective characteristic of maturity. Apparently the new health education was such a development. The ambitious proposal for medical health supervision of all children through the schools now appears to have been merely a dream that would involve the schools in more service than they could deliver. It presumed that the schools could give such individual preventive pediatric advice and supervision as is likely to be possible only for those who can afford an abundance of medical care. The recommendation of a trained full-time director for a centralized supervision of all phases of the health program appears to have been one of the essentials of maturity which was clearly visualized very early. Its accomplishment for any large proportion of the school systems will come only as the inefficiencies and gropings of the adolescent period are passed and the developed form of the program is seen by all public officials responsible for the schools and public health.

The Hoover White House Conference has collected consensuses of opinion generally.[12] Further evidence of the situation today is shown in numerous surveys and in reviews of state and city annual reports. These all show that the medical and nursing services in the schools continue to emphasize the control of contagion, the correction of physical defects; and when they have wise direction, they aim at a better coordination of the medical and nursing service with the health teaching in the classroom. Medical care or correction of defects is recognized as outside the scope of the school program by the leaders, but hard work is ahead to keep the schools from extending treatment services.

We have had the physician and the nurse in the schools long enough so that the public, the teachers, the administrative officers, and the boards of education would not do without their assistance. They want to know the physically handicapped children. They want the medically neglected child cared for. They want advice and assistance when communicable disease threatens. Any school staff which has had a little of their assistance wants more than can be supplied. This demand has led to a practice of rapid selection of children who seem to need medical care. This practice has been almost universally used for over twenty years. The need for this screening service is established, but the method of screening has been extravagant and ineffective. It has used the physicians to follow routines that are wasteful and unscientific. It has been the horrible example of the physician employed by a government agency. The physician, pressed by lay officials to see more children than he can effectively examine or appraise, obviously violates the principles laid down by the House of Delegates of the American Medical Association.[13] "The responsibility for the character of medical service" has not been "borne by the profession." The operation of the service has not been according to medical standards. "We have allowed the demand for seeing large numbers to lead us into hasty

and dubious judgments instead of adhering to the principle that "the medical profession alone can determine the adequacy and character of medical service." We have allowed the public or the school authorities to push us into attempting hasty judgments that we know were not based on sound medical standards.

This indictment of school medical examinations needs no elaborate evidence of current practice. Thousands of physicians who have tried conscientiously to render this service have testified to the hasty and unsatisfactory examinations they have been required to make. Many have given it up in disgust. Thousands more now engaged in this work are willing to give similar testimony but are unable to change the system. There is sufficient recognition of the unsatisfactory character of the medical and nursing service in the schools by educational and public health leaders to insure a cooperative response for well-considered plans for improvement. There is a tendency to return to the early objectives of protecting the schools against waste and of promoting health through control of communicable disease and the follow-up and advice to care for handicapping physical defects. We find more willingness to return to the early objectives in order to improve the work we started out to do twenty years ago.

The Medical Service Section of the White House Conference makes clear the limited applicability of the school examination.[14] This Section indicates that a judgment of a child's particular needs can be formed only after consideration of many factors which include hereditary endowment, the nature of his environment, and his total structural and functional adequacy. Thus the routine methods of the school examination cannot be relied upon, except in very restricted fields, for recommendations to parents. This committee reported the finding of defects, as is done in school, and the attempts made to have these defects corrected have most commonly led to unwarranted activities. This recognition of the tendency for the schools to attempt to expand beyond their proper sphere of activity and therefore to return now to the earlier objectives of school medical inspection is, it seems to this Committee, one of the definite evidences of a sound development of the school health program.

There is a further problem, however, which was ably stated by the Report of the New York State Health Commission[15]: "The physical examinations which are made each year of every school child represent useless expenditures unless steps are taken to correct the defects found. Hundreds of thousands of dollars are spent annually in the state for the examination and reexamination of children which discover and rediscover the presence of defects about which nothing is done either by the parents or by the school. . . . Future efforts to promote the health of school children should be directed toward securing the necessary care and treatment rather than the routine reexaminations." A significant contribution to determine why definitely serious defects are not adequately cared for was made by a research reported last year. This was a study conducted by the Research Division of the American Child Health Association supervised by a special advisory committee and financed by the Metropolitan Life Insurance Company. The chairman of the Advisory Committee was Dr. Philip Van Ingen, an active Fellow of the Academy, and a member of this Committee was the medical representative on the staff making the study. Dr. Charles Hendee Smith, and Dr. Edwin A. Riesenfield gave further pediatric representation to this research. The limited applicability of school examinations expressed by the Medical Service Section of the White House Conference was given added force by the findings of this research. One of the important causes of failure to obtain corrections of defects was found to be the character of the examinations which cannot be relied upon for recommendations to parents. As a result of this research it was suggested that screening devices, developed through research, be used to select the children most likely to be in need of medical care or to make preliminary selection

of cases who would later be referred to the physician. "Delegating this preliminary culling of children to other members of the school staff would very largely free the school physician from this task and allow him to give much more careful examinations to those who have already been selected by the screening process. His recommendations on the smaller number would then be the result of careful consideration of each child rather than a hurried judgment with limited evidence on a large number of children."[16] This suggestion meets the need for accurate selection of cases requiring persistent follow-up to avoid the neglect referred to in the New York State Report. It also avoids the unwarranted activities mentioned by the Medical Service Section of the White House Conference.

A further contribution to school medical inspection service came out of this research in the principle: "The available facilities both for follow-up and correction should be considered in determining the severity of a selection for follow-up." This principle is concerned with the correction facilities for those children whose parents are not able to pay for medical care. In cases in which the full cost of medical care cannot be provided for every child, it is only reasonable that the more serious cases should be given first attention. There is no point in discovering defects requiring free care year after year if we cannot serve them. Likewise, there is no good reason to find more defects for follow-up than can be followed through to a satisfactory termination. To make a proper use of the facilities for correction and follow-up, the severity of each case must be considered.

RÉSUMÉ

The growth and development of the school health program during forty years has progressed from the rapidly changing period of infancy through a childhood that maintained a steady increase in size through the addition of more and more special personnel. The period of adolescence came during the War and the prosperous years that followed. This latter period was characterized by such ambitious schemes and visions of the future as is common in adolescence. Today, many of the schemes have been sufficiently evaluated to give guidance for the future.

RECOMMENDATIONS

A review of the history of school medical inspection indicates sufficient experience, survey, opinion organized through group conferences, and research to indicate some of the objectives and principles that should give guidance to those concerned with school health programs. The responsibility for the character of medical service should be borne by the medical profession, who alone can determine its adequacy and character.

It is the feeling of this Committee that further study by them may result in the development of such clarification of the objectives and principles of school medical service as will aid each pediatrician to give guidance and leadership in the improvement of the service in his own community.

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16. Physical Defects—The Pathway to Correction, American Child Health Association, New York, 1934, p. 116.

Transactions

FOURTH ANNUAL MEETING OF REGION IV OF THE AMERICAN ACADEMY OF PEDIATRICS

A joint meeting of Region IV of the Academy of Pediatrics and the North Pacific Pediatric Society was held in Seattle, August 9 and 10. Region IV of the Academy includes western Canada and the western states. Sixty pediatricians attended, among them Dr. Henry Dietrich, of Los Angeles, president; Dr. Clifford Grulee, of Chicago, secretary; and Dr. Edward B. Shaw, of San Francisco, regional director of the Academy.

Friday evening the annual banquet was held at the Inglewood Country Club, and Saturday afternoon a trip by boat was taken along the Seattle water front, through the government locks into Lake Union with an hour's trip about Lake Washington. The boat trip concluded with a buffet dinner at the Seattle Tennis Club.

Following the papers on Friday afternoon the state committeemen met with Dr. Shaw for a short business session in connection with regional work of the Academy.

During this meeting Dr. Edith P. Sappington, of San Francisco, western representative for United States Children's Bureau, gave a brief discussion of "The Tentative Outline for State Plan for Maternal and Child Health," with further brief discussion of a proposed plan for crippled children. Plans are being made for the Academy to enter into the above work, which should be under medical rather than political control.

An examination of applicants for certification as pediatric specialists was held the day preceding the meeting, and Dr. Borden S. Veeder, of St. Louis, and Dr. Franklin P. Gengenbach, of Denver, who represented the American Board of Pediatrics, remained and took part in the program.

Treatment of Staphylococcus Aureus Osteomyelitis and Septicemia With Neosalvarsan. Edward LeCocq, Seattle, Wash.

In a series of 27 cases, 19 positive blood cultures were found, and 9 deaths occurred. By the use of neosalvarsan, the mortality rate was reduced from 85 per cent to 25 per cent. The effectiveness of the drug was tested in the laboratory and it was found that neosalvarsan destroyed the *Staphylococcus aureus* in dilutions of 1:100, was inhibitory in dilutions of 1:100 to 1:1,000, but in greater dilutions than this had no effect on the organism.

Celiac Disease. Intestinal Absorption and Gastrointestinal Motility. Arthur E. Wade, Seattle, Wash.

Two cases of severe celiac disease were studied from the standpoint of observation for new symptoms and new response to physiologic treatment.

Both cases presented the accepted symptoms which follow the initial devastating diarrhea. (1) Large abdomen in contrast to the striking emaciation of extremities and buttocks; (2) failure to gain height and weight; (3) numerous daily stools of a porridge-like consistency, voluminous in size, and with the characteristic celiac odor; (4) flat blood sugar curve; (5) backward in speech but precocious in understanding; and (6) secondary anemia.

In addition to the above were found the following symptoms: (1) night weight loss of two to three pounds; (2) urine, sp. gr. 1.006-1.010; (3) two-thirds of the twenty-four-hour amount of urine was passed between 7 P.M. and 7 A.M.; (4) urine concentration tests failed to bring a response; (5) little intestinal peristalsis was heard; and (6) barium meal gastrointestinal x-ray study showed the stomach one-third full at eight hours and unpassed barium in the sigmoid at ninety-six hours.

In view of the feeble intestinal peristalsis and the prolonged stay of the barium in the tract, posterior pituitary was given by hypodermic in doses of 5 minims twice daily to act as an intestinal peristalsis stimulant. The following results occurred: (1) the night weight loss was reduced to from ½ to 1¼ pounds; (2) urine, sp. gr. 1.016-1.020; (3) one-third of the twenty-four-hour quantity of urine was passed between 7 P.M. and 7 A.M.; (4) urine concentration tests showed fair response; (5) normal peristalsis could be heard; (6) barium meal gastrointestinal x-ray study showed a normal emptying of stomach and intestine (all barium passed in twenty-four hours); (7) blood sugar curve normal; (8) formed stools; (9) immediate weight gain (one child who had been stationary in weight for two years gained four pounds in nine days); (10) appetite and general sense of well-being improved.

Discontinuance of the pituitary treatment caused both children to lapse into their former celiac condition. Laxatives were used as the peristaltic stimulant with the same result.

It is to be noted that when intestinal peristalsis was normal, intestinal absorption was normal and that when intestinal peristalsis was normal, the high protein plus the conventional banana diet was not necessarily needed.

An hypothesis is suggested from this study. In celiac disease the normal gastrointestinal motility has in some way been largely suspended and intestinal absorption reduced nearly to the laws of osmosis and filtration—thus the gastrointestinal tract becomes a great reservoir containing vast quantities of digested but unabsorbed food elements and water. A stimulation of peristalsis restores absorption and the normal blood food waves. It is during the food wave as indicated by blood food curves that metabolism stores the reserve depots.

End-Results in Celiac Disease. A. Howard Spohn, Vancouver, B. C.

The survey of children suffering from celiac disease was undertaken from eight to ten years after the onset of the disease. It comprises a report of sixteen cases, twelve being in females, and four in males.

A history of an acute infection, such as measles, influenza, or dysentery, had been found occurring a short time before the clinical symptoms of celiac disease appeared. In all but one case, the health and development of these children had been normal before the infection and subsequent celiac disease.

The usual high protein diet was given in all cases.

In a number of cases, small doses of insulin were given over an extended period, in some cases as long as two years. It appeared that in these cases insulin was a useful adjunct in treatment, improving the appetite, decreasing the abdominal distention, and enabling more carbohydrate to be given in the diet. It appears that carbohydrate in the form of glucose can be given in larger amounts than formerly thought possible.

In two cases celiac disease was associated with extreme rickets, after three years of age, following acute infections of measles and influenza in one child with normal development. The photographs of the child at the age of three years showed normal development, and subsequently extreme deformities of the chest, arms, legs, and spine appeared.

The teeth of practically all these children showed only the usual signs of decay.

The stationary growth over a long period was present in all cases. Those who have reached adolescence have attained the stature of their parents, and the girls in all cases are taller than their mothers.

Death occurred in only one case, and this was due to long-continued refusal on the part of the mother to adhere to any prescribed treatment. Autopsy showed the usual findings seen in deaths from starvation.

The clinical symptoms in many ways resemble those seen in adults suffering from sprue. Recurring ulcers in the mouth were present in several cases. In one case ulceration of the mouth appeared at the onset and reappeared for a long period with each setback.

Mumps Meningitis and Meningoencephalitis. L. Howard Smith, Portland, Ore.

A rather high incidence of central nervous system involvement occurred in a recent epidemic of mumps in and about Portland. Six cases received hospital study with recording of spinal fluid and laboratory findings. Five were of the meningitis type—coincident with the onset of the parotid swelling or from one to seven days after there was headache, vomiting, often delirium and fever, rigidity of the neck, positive Kernig sign, and increased reflexes. The cerebrospinal fluid, under increased pressure, was clear and showed a cell count for 119 to 555 with lymphocytes predominating. Each of the five patients made a complete recovery in a few days. In one case of the encephalitis type, the patient continued for two weeks in a comatose condition with high temperature from 104° to 106.8° F. and with marked spasticity of both arms and legs. Recovery was slow and gradual.

Nine other cases not receiving hospital care but which clinically must be considered as mumps meningoencephalitis were also reported. All recovered.

A striking feature of mumps meningoencephalitis is the preponderance of males affected. Of the 15 cases reported, 13 were males and only 2 females. In collecting 44 cases from the literature of the last ten years, 81.8 per cent were male and 18.2 per cent female. This fact has not been noted in any of the literature reviewed.

Motor Dysfunction of Right Half of Colon of Congenital Origin in Children. W. H. Buecrmann, Portland, Ore.

Acute Poliomyelitis. Observations on Cases Among Children in Spokane and Vicinity in 1934. E. J. Barnett, and C. L. Lyon, Spokane, Wash.

From May to November, 1934, there were 161 cases of acute poliomyelitis reported in Spokane County, with nine deaths (5.6 per cent). Of these, 119 (75 per cent) were fifteen years of age or younger. A fair cross-section of the disease in this locality can be obtained by a study of the forty-four cases under our care.

The majority of cases were seen in July and August. Refusal to attempt "contact" immunization seemed justified in view of the fact that none of sixty-one well children living in "infected" homes contracted the disease. There were no reported cases among nurses or doctors.

The incidence of males to females was 3 to 1. The symptomatology was fairly constant with a sudden onset, fever, headache, and sore throat. The most consistent and significant finding was a stiff spine. The fever persisted for four days or less. Tremor, restlessness, anxiety, and excitement were often observed. The average spinal fluid cell count was 138, the lowest being 28 and the highest 650. The cell count was of no value in prognosis. Less than one-half of the group, 20 (46 per cent), were of the abortive or nonparalytic type, whereas 24 (54 per cent) developed definite paralysis. (In the California epidemic the incidence of abortive to paralytic

cases was estimated from 10:1 to 50:1.) Of the 29 children given serum (20 c.c. pooled convalescent) in the preparalytic stage with positive spinal fluid findings, 9 children became paralyzed, and in 1 child the paralysis remained severe and permanent. Of the 14 children seen after paralysis, 3 still show spinal paralysis.

It is most difficult to draw conclusions from the use of serum in this outbreak. Following the use of serum there were 20 nonparalyzed children, and of the 9 paralyzed, only 1 severely so. On the other hand, of the 14 children paralyzed when first seen, in only 1 was the paralysis disabling. How many of the 20 nonparalyzed children would have escaped paralysis without serum injection? Was the relief as much from the spinal fluid drainage as from the serum? Was the single small dose of serum really efficacious or would the incidence of abortive cases have been the same without serum?

The outbreak was not mild from the standpoint of the number of cases of paralysis (54 per cent) but was unusually mild from the number of deaths and the lack of permanent paralysis. Acute poliomyelitis appears so changeable with each recurrent outbreak in the same community and even with the same epidemic in separate localities that accurate conclusions with reference to serum treatment may always be questionable.

Cleft Lip and Palate. Herbert E. Coe, Seattle, Wash.

The first operation is done on the lip when the child has reached the weight of 12 pounds. Preliminary strapping of the lip with adhesive plaster should be begun soon after birth and continued until the time of the first operation. Tight strapping narrows the cleft in the alveolus, improves the shape of the ala, and stimulates growth of the lip. Kerosene is less irritating than benzine or ether for removing the adhesive. The use of a nipple in feeding should be avoided as it tends to spread the cleft in the palate. A spoon, a bit of small tubing on the end of a 10 c.c. syringe, or a Breck feeder with a large opening is recommended. The child should be held at an angle of about 45 degrees, and much patience is necessary in feeding. Cleft palate nipples have not proved to be satisfactory.

These children are particularly susceptible to colds. An even room temperature should be maintained and warm saline irrigations used rather than the usual nasal antiseptics.

Many operations are required. The sequence of operations is: the lip, the soft palate, the hard palate, and finally the alveolar gap. Secondary operations are usually necessary to improve the appearance of the nostril or lip margin.

Skilled, special nursing is most essential. The lip scar is usually inconspicuous, but it is difficult to obtain a perfect nostril. Scarring is more frequently due to radical extensive surgery than to multiple carefully performed operations. Speech is always defective at first, even when the palate is closed early, but gradually improves under careful persistent training until it may be practically perfect. A careful study is being made of the influence of heredity as an etiologic factor.

Whither Pediatrics. Franklin P. Gengenbach, Denver, Colo.

Possibilities of Blood Transfusion in Pneumonia. W. B. Seelye, Seattle, Wash.

A three-year-old boy ran a rather stormy course for two weeks with a bronchopneumonia. His temperature fluctuated as much as eight degrees Fahrenheit in twenty-four hours. There was no evidence of resolution or healing taking place in the lung. One hundred fifty cubic centimeters of citrated whole blood were given intravenously, and within twenty-four hours his temperature had dropped to normal where it remained from then on.

While no conclusions can be drawn from a single case, may we not consider blood transfusion as worth while in certain cases of pneumonia?

Chronic Arthritis in Early Childhood. H. L. Moon, Seattle, Wash.

Allergy as the Cause of Frequent Colds and Persistent Cough. Norman W. Clein, Seattle, Wash.

A female child, six years old, had "always had a poor appetite" and frequent colds since birth. The colds terminated in a persistent cough. Since pertussis at three years of age, wheezing has been present at times with the cough. The mother has had "chronic nasal catarrh."

Nasal congestion, with a watery discharge, is always worse in the morning (typical of allergic rhinitis). Mouth-breathing was always present and was not relieved following a tonsil and adenoid operation.

Physical and laboratory examinations were normal except that the nasal smear showed an eosinophilia of 50 per cent (pathognomonic of allergy). Complete skin testing revealed a marked sensitivity to wheat, cheese, orange, cauliflower, spinach, pork, house dust, and orris root. Grass pollen tests were all positive. Eight intradermal tests were given to verify some of the positive tests.

Treatment consisted of (1) elimination of positive foods, (2) environmental control, (3) mixed grass pollen desensitization (four daily injections, a total of 0.8 c.c. of 1:50,000 vaccine, gave complete relief).

The child feels better than at any time in her life; her appetite is very good; and she is very happy.

Pigmented Naevi. Herbert E. Coe, Seattle, Wash.

Epidemic of Diarrhea in a Hospital Nursery Apparently Caused by a Monilium. Jay I. Durand, Seattle, Wash.

Twenty-three cases occurred in the nursery of one of the local hospitals between January 14 and June 24 with nine recoveries and fourteen deaths. Upon careful search none of the organisms known to cause such an epidemic were found by any of the three laboratories, in which studies of the stools were made. However, in June highly refractile spores, somewhat smaller than a red blood cell, were recognized in one of the cases. These were found in all of the last four cases which occurred. The same organism was found in the glucose used for making the solutions in the nursery. The organism had the appearance of a yeast or monilium. After changing the glucose, disinfecting, and cleaning up the nursery, no new cases occurred. The diarrhea was characterized by yellow, fermentative, very acid stools. Blood was never found. The patients showed extreme dehydration, low temperatures, and distention of the abdomen. Death occurred in two to ten days' time.

Autopsies showed nothing except mild injection of the mucous membrane, with no ulceration.

Errors in Cardiac Diagnosis. R. H. Somers, Seattle, Wash.

Sudden Death in a Case of Obstruction of the Urethra, With Dilatation of the Ureter, Accompanied by Large Adrenals. V. W. Spickard, Seattle, Wash.

A male child, twenty-three months old, for one month suffered loss of appetite, loss of weight, constipation, frequency of urination, and attacks of pallor with air hunger. The child showed constant pyuria. He was in the hospital for a month

being treated for pyuria. He was brought to the office for examination. After being undressed and weighed and just before he was to be examined, he appeared to be frightened, developed gasping breathing, turned pale, and assumed an extremely anxious expression. The breathing became slower, and he expired in a few minutes in spite of all attempts to revive him.

Diagnosis: Apparent obstruction of the urethra of congenital origin, with dilatation of the urinary bladder, ureter, and pelvis, with associated nephritic change in the small amount of remaining kidney tissue? The adrenal was enormously enlarged on both sides with adenomatous change of cortical portion and hypertrophy of the medullary tissue. The adrenals were much larger than the remaining kidney substance. It was felt that the sudden death was due to hyperadrenalism.

"Dry Ice" Treatment of Hemangiomas. H. T. Clay, Tacoma, Wash.

This demonstration is for the purpose of showing the use of commercial "dry ice" or carbon dioxide ice in the treatment of hemangiomas in children. Its advantages lie in its availability, adaptability, and cheapness. Although the temperature is −110°, it can be kept about the office for three or four hours if it is well wrapped.

The technic consists in the application of the ice with firm pressure for twenty to sixty seconds, according to the size of the lesion. The surrounding skin is protected by blotting paper. A vesicle results which heals in about two weeks. Infection has not occurred. Cosmetic results are very satisfactory.

Discoloration of Teeth Following Icterus of Newborn. John D. Fuller, Seattle, Wash.

Three cases of permanent staining of the infant teeth, apparently related to an icterus neonatorum, are reported. In each instance the staining has been pronounced by dentists to be of both enamel and dentine and has been continuously present since eruption.

Such green staining of the first teeth has not been previously reported in dental or medical literature. All cases occurred in one locality. Sections are to be made as soon as it is possible to obtain one of the teeth. It is suggested that some factor in the maternal diet or the child's blood chemistry caused the production of an insoluble bilirubin, biliverdin, or porphyria pigment. It is not possible at this time to venture an opinion as to whether the exciting cause is hereditary, dietary, or glandular, but it is significant to note that all patients showed evidences of pituitary dysfunction, and all were of mothers living in a country notoriously lacking in certain salts, notably calcium and iodine.

Hemolytic Streptococcus Blood Stream Infection With Severe Complications and Recovery. Armin Rembe, Seattle, Wash.

R. H., aged ten years, was seen at home with a swollen, inflamed, tender right foot with a small draining area on the plantar surface. There was a history of running a thorn in the foot while swimming five days before. There was no fever. The child, critically ill, was admitted to Swedish Hospital with temperature of 105° F., and pain in the chest. Blood culture was positive for hemolytic streptococcus. Physical and x-ray findings showed pneumonia in the left chest—severe coughing paroxysms.

There was definite pericardial friction rub.

Heart sounds were distant, with much dyspnea and cyanosis. X-ray examination confirmed rapid pericardial fluid accumulation; 200 c.c. of brownish, thin fluid removed from pericardial sac. Dyspnea and cyanosis were relieved. Examination of

fluid showed many pus cells and culture was positive for *Streptococcus hemolyticus.*

Treatment consisted of use of an oxygen tent and periodical small transfusions of 200 c.c. citrated blood. Digitalis and other diuretics did not increase the output. Salyrgan, intravenously in 1 c.c. doses, was of definite help in increasing elimination. No antistreptococcus serum was given.

The child apparently made a complete recovery. He has no apparent permanent cardiac damage, although he will require many months of rest because of the myocardial and pericardial involvement.

Nephritis. C. Luverne Smith, Seattle, Wash.

A twelve-year-old boy was admitted in the state of coma, with a diagnosis of nephritis. There was no recent history obtainable of acute infection, but child had many attacks of sore throat up until three years before, when tonsils were removed. He had S.P. three years ago, but there was no history of scarlet fever or diphtheria.

This case is presented as a case of hemorrhagic nephritis. The patient was admitted in acute uremia, and his life was probably saved by prompt and vigorous treatment. He later progressed to apparently complete recovery.

Academy News

The following committees have been appointed by President Dietrich on the recommendation of the Executive Board.

Nominating Committee:

Chairman, Dr. Thomas B. Cooley, Detroit, Mich.
Dr. Hugh Leslie Moore, Dallas, Texas
Dr. Edgar P. Copeland, Washington, D. C.
Dr. Joseph B. Bilderback, Portland, Ore.

Committee on Legislation:

Chairman, Dr. Jos. S. Wall, Washington, D. C.
Dr. Jay I. Durand, Seattle, Wash.
Dr. Isaac A. Abt, Chicago, Ill.
Dr. Alfred Walker, Birmingham, Ala.
Dr. Philip Van Ingen, New York City

Committee on Allocation of Research Funds:

Chairman, Dr. Kenneth Blackfan, Boston, Mass.
Dr. Fritz Talbot, Boston, Mass.
Dr. Irvine McQuarrie, Minneapolis, Minn.
Dr. A. F. Hartmann, St. Louis, Mo.
Dr. Thomas B. Cooley, Detroit, Mich.

Dr. Edgar E. Martmer of Detroit has accepted the state chairmanship for Michigan.

Dr. Morgan Smith of Little Rock, Ark., died recently. Dr. Smith was graduated from Tulane University in 1904 and has been engaged in the practice of pediatrics in Little Rock ever since. For many years he has been Professor of Fediatrics at the University of Arkansas.

Dr. Smith was looked upon as an outstanding man from many angles. He served in the state legislature for several terms and was unquestionably the leading man in pediatrics and pediatric efforts in Arkansas. In his death American pediatrics has lost a diligent worker and an outstanding character.

Book Review

Nutrition Work With Children. LYDIA J. ROBERTS, University of Chicago Press, 1935, revised and enlarged second edition, 639 pages. Price, $4.00.

This book is one of a series issued by the University of Chicago to cover the matter included in the courses given in the Department of Home Economics. The series is planned with the purpose of supplying suitable textbooks for corresponding courses in other institutions and secondary schools, and of making available to the general reader and especially to the educated homemaker, material now often limited to the classroom. During the nine-year interim since the first edition was prepared, notable advances have been made in almost every field, and a remarkable output of basic research from nutrition laboratories over the country has given new light to many fundamental nutrition problems. All these developments and influences have been given recognition in the present revision.

Chapters I, II, and III, which are on the need for nutrition work, its purpose and scope, a definition of terms whereby the true meaning of nutrition and malnutrition is defined and described, and methods of judging nutrition, have been practically rewritten in order to reflect the recent advances and increase of information. An important discussion of studies on growth is presented in Chapters IV and V. These first five chapters have three important features: first, they have great interest to medical men in general and to pediatricians in particular; second, the published work about which there has been considerable controversy is analyzed and assessed in a critical and conservative manner, and third, the material included is of great informational value.

Chapters VI, VII, and VIII discuss the causes and mental and physical effects of malnutrition. In Chapter VII two new discussions have been included; one deals with the effects of the depression on nutrition and health, so far as they are known at present; the other is a summary of some of the outstanding studies that have demonstrated the effects of optimum versus adequate nutrition. Chapter VIII is an expanded discussion of the mental effects of malnutrition. The final chapter of medical interest is Chapter IX on the prevention and treatment of malnutrition.

In the remaining eight chapters, the second half of the book, the relationship of schools and agencies interested in health and parent education to nutrition is presented. The nutrition-health program and teaching in the schools at various age levels, the responsibility of different workers in the program, and special school problems are discussed.

An excellent full bibliography is included at the end of each section. Also at the end of many sections the author presents a summary of the material included in that section with an evaluation of conflicting and ill-defined ideas. No diets are included, and this is no "cook book."

The author's training and position make her preeminently fitted to undertake the preparation of such a book and especially to discuss the material and problems included in the text. She has done this successfully and in a manner which makes the book pleasant and easy to read, and extremely useful to medical men interested in this field of pediatric activity, whether or not they are specially trained to carry on investigative work in the problems concerned.

H. McC.

Comments

COMPLEMENT IN THE SERUM TREATMENT OF MENINGOCOCCUS MENINGITIS

IT HAS long been known that complement is absent from normal cerebrospinal fluid. In 1908 M'Kenzie and Martin[1] noted an absence of complement in the cerebrospinal fluid of a few cases of meningococcus meningitis. They also studied the bactericidal effect of human serums on meningococci. It was found that the serum of normal individuals, patients with acute and chronic meningitis, and patients who had recovered had some bactericidal effect. It was much greater in patients who had recovered. They found that the bacteriolytic action depended on a thermostable immune body which required the presence of thermolabile complement to complete the process. Davis[2] had previously shown that normal human serum was distinctly bactericidal for the meningococcus and that this property was diminished but not entirely destroyed by heating the serum to 60° C. for thirty minutes.

Kolmer, Toyama and Matsunami[3] and Matsunami and Kolmer[4] found that normal serum or complement increased the opsonic activity of commercial antimeningococcus serum. They recommended the addition of 1 c.c. of fresh, sterile human or guinea pig serum to each 9 c.c. of antimeningococcus serum. Evans[5] was unable to confirm these observations. This investigator did not observe any reactivating effect when complement was added to commercial serum.

In connection with the above recommendation of Kolmer, it would seem that, even if complement were necessary or of value, 1 c.c. of normal serum as complement would be an insignificant amount. Such a small amount would be diluted out of the range of activity by the cerebrospinal fluid.

Also it should be pointed out that most human serums (adult) have definite, though slight, meningococcidal power. This has been shown by numerous observers including Davis,[2] M'Kenzie and Martin,[1] Matsunami and Kolmer,[4] Matsunami,[6] Heist, S. Solis-Cohen and M. Solis-Cohen,[7] and Silverthorne and Fraser.[8] For this reason, the activity of fresh human serum, especially from an individual convalescent from meningococcus meningitis, may be due, in part, at least, to a thermostable immune body and not complement.

In 1932 Ward and Fothergill[9] commented on the frequent absence of complement in the cerebrospinal fluid of patients with influenza bacillus meningitis, and reported five cases of this disease which were treated with a mixture of antiserum and complement. In addition to this, Ward and Wright[10] presented data describing the immune mechanism involved in the serum destruction of meningitic strains of influenza bacilli and the rôle played by complement in such a mechanism. Briefly, the latter authors observed, in test tube bactericidal experiments, the following results:

A. Inactivated immune influenzal serum plus virulent influenza bacilli (meningitic strain) resulted in practically no bactericidal action.

B. Inactivated immune influenzal serum plus virulent influenza bacilli plus fresh, normal serum (complement, i.e., infant's blood) resulted in good bactericidal action.

C. Inactivated immune influenzal serum plus virulent influenza bacilli plus washed defibrinated blood cells resulted in very little bactericidal action.

From these observations it appears that the immune mechanism involved in the serum destruction of influenza bacilli is largely a complemental bacteriolysis with phagocytosis playing little or no rôle. On the contrary, the mechanism involved in the destruction of meningococci is largely a phagocytosis of sensitized organisms. In this latter type of immune mechanism, as has been shown by Ward and Enders[11] with reference to the pneumococcus, complement is not essential but may accelerate the reaction.

In 1916 Fairley and Stewart[12] treated ten cases of meningococcus meningitis by adding fresh, human (convalescent) serum to the antimeningococcus serum. Seven of the patients recovered. Then again, in 1933, Bunim and Wies[13] reported a single case of meningococcus meningitis with recovery following the use of complement. Their observations were sufficiently controlled to suggest that complement possibly was a factor in the recovery of their patient.

In 1933 Fothergill[14] reviewed the general problem of the treatment of influenza bacillus meningitis with antiserum and complement. Brief mention was made of nine cases with recovery. Rittenberg[15] in 1934 reported a single case of influenza bacillus meningitis with recovery following the use of antiserum and complement. Pittman[16] has also reported the use of complement and antiserum in the treatment of a few cases of influenza bacillus meningitis. In connection with these reports regarding influenza bacillus meningitis, it should be repeated that the immune mechanism here concerned is different from that involved in the destruction of meningococci.

Recently Fothergill[17] presented observations on the presence of complement in the cerebrospinal fluid of patients with various acute inflammatory conditions of the central nervous system. The presence of complement in such fluids is extremely variable. It is present in a small percentage of the cerebrospinal fluids of patients with meningococcus meningitis.

From the above review, with reference to meningococcus meningitis, it can be seen that: complement is not essential in the immune mechanism resulting in the destruction of meningococci; complement is occasionally present in the cerebrospinal fluid of patients with the disease; and, normal, fresh, human serum is frequently meningococcidal irrespective of its complement content. We have tested the cerebrospinal fluid of several patients with meningococcus meningitis for the presence of complement every time a lumbar puncture was made for serum administration. At no time during the course of the disease was complement present, and yet these patients made complete recoveries. It is almost trite to point out that complement has seldom been used in the past; nevertheless, the mortality in properly treated meningococcus meningitis has been considerably reduced. It should be emphasized that the *first essential* in the treatment of meningococcus meningitis is the intrathecal use of a potent immune serum *specific for the type of meningococcus infecting the patient.*

From what has been said it should be obvious that from a practical point of view the use of complement in the serum treatment of meningococcus meningitis not only is unnecessary but may result in "harmful" treatment to patients with this disease in that its use may quantitatively replace, to a certain extent, a more potent form of therapy. In the review of the literature which has been cited, there is no conclusive evidence that the use of complement particularly enhances the value of a properly chosen serum; yet there appear from time to time in the literature beneficial claims for this additive substance. Recently, Fondé[18] reported two cases in which he concludes that the use of fresh, human serum in combination with antiserum effectively influenced the action of the serum—in other words, the implication is made that the success in these two cases was due to the addition of complement to the serum. In a critical analysis of this paper, it appears that this conclusion

is based on very meager data. Commercial antimeningococcus serum was used, and no data are presented to show that it was specific for the strain of organism infecting his patients. As complement, serum from an individual recently recovered from meningococcus meningitis was used. It was not shown by bactericidal experiments that the effect of this serum was due to complement rather than a thermostable immune body. Tests are not cited to show that complement was not present in the cerebrospinal fluids of these patients. There is no justification on the basis of the evidence presented for Fondé's conclusion that "the use of fresh human serum intraspinally is a distinctly valuable addition to the serotherapy of meningococcus meningitis."

Fondé used complement alternately with antiserum which (even if there was value in complement) is not a logical procedure. When complement is injected intrathecally, it may disappear rather quickly because of dilution by the cerebrospinal fluid and because of absorption. We have injected as much as 15 c.c. of complement intrathecally in patients with influenza bacillus meningitis, and we could not detect it in cerebrospinal fluid withdrawn only four hours later. Therefore, if complement is to be used, it should be mixed directly with the antiserum.

We can summarize this question as follows: There is no evidence so far to show that it is necessary to provide complement in the treatment of meningococcus meningitis. Nor can it be completely denied that it may be useful in an occasional case. However, before one is justified in concluding that it is helpful, in any case in which it may be used, the following facts must be known:

A. The patient must have been treated with a potent serum, serologically specific for the strain of organism infecting him.

B. Under such treatment it must have been demonstrated *by culture* that the infection is continuing.

C. It should be realized that such continued infection may be due to an isolated focus of infection such as a pyoventriculitis or a walled-off subarachnoid lesion or to persisting meningococcemia.

D. It must have been demonstrated that complement was continually absent from the cerebrospinal fluid.

E. The above data all being known, it must then have been demonstrated that the addition of complement to the antiserum resulted in prompt sterilization of the cerebrospinal fluid.

F. It must have been demonstrated by bactericidal experiments that the activity of the fresh normal serum used as complement was due to complement per se and not due to the presence of *thermostable immune bodies.*

Unless the above criteria are properly satisfied in each individual patient, we would be unwilling to accept the possibility that complement was a factor in the recovery of a patient with meningococcus meningitis treated with antiserum and complement.

SUMMARY

A review is presented of the use of complement in the treatment of meningococcus meningitis.

Criteria are outlined which should be fulfilled before one can conclude that the use of complement in addition to antiserum is responsible for recovery in a patient with meningococcus meningitis.

In our own experience with meningococcus meningitis where these criteria have been fulfilled we have been unable to conclude that complement has been of any therapeutic value.

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The Journal of Pediatrics

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